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PHYSIOLOGY AND FUNCTIONAL PATHOLOGY OF THE LYMPHATIC SYSTEM APPLIED TO ALLERGY OF THE NOSE AND PARANASAL SINUSES*†‡

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STAGNATION of tissue fluid is a constant pathologic finding in allergic disease of the nose and paranasal sinuses. Since the lymphatic system is primarily concerned with removal of certain components of extravascular fluid, alterations of its activities are important in the pathogenesis of allergic disease. This discussion considers the phylogenetic development of the lymphatic system, certain principles of physiology and functional pathology of the sinus mucosa, and application of these principles to various types of sinusitis. Included is a brief description of the therapeutic application of local pressure to the mucosa of the maxillary sinus.

PHYLOGENETIC DEVELOPMENT

The lymphatic system develops in the phylogenetic scale of life as it becomes necessary to remove from the body substances not readily absorbed by the blood. It develops as a constantly changing pericellular environment and becomes essentially an excretory system for the products of cell metabolism and food (protein) unused by the body cells.[1] A brief résumé of this process follows.

Every living cell requires food and an excretory mechanism. Also, as a characteristic of life, it possesses some type of membrane permeability and motion. Its motion may be either that of molecular diffusion (intracellular and transcellular motion), physical movement, or both. The amoeba lives by molecular diffusion through its covering membrane and by accretion and excretion through pseudopodia. Its pseudopodia also are used to carry it away when its environment becomes saturated with its excretory products. The slightly higher developed flagellated unicellular organisms (*Paramecium*)

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leave their excretory products behind them by locomotion. If sedentary (shellfish), they create their own currents by cilia or depend for a change of environment upon the currents of their habitat, such as tides or flowing streams. The necessity for these extracellular currents is evident in the spawning habits of fish. Some spawn only in flowing water and can leave their eggs, whereas pond fish must remain over their eggs and create a current with their fins or keep their eggs attached to their bodies and provide changing pericellular environment by their locomotion.

The first lymphatic system consisted of a constant change in the environment of the organism. Sea water bathed the exterior of the organism or entered the body through portals to carry away the excretory products. As the complexity of life increased, the portals became closed so that the most primitive closed circulatory system contained a fluid identical with the sea water in which the organism lived. This characteristic, in so far as the crystalloid solutes of the blood is concerned, still obtains in all vertebrates, i. e., all vertebrates contain the same percentage of salts in their plasma as was present in the sea water during the era when their ancestors' circulation became closed.[2]

In the lower vertebrates (fish, amphibia, reptiles), as the circulation becomes differentiated into intra- and extravascular fluids, lymph hearts appear to establish a current in the extravascular fluids which bathe the body cells. These creatures die of tissue fluid stagnation if their lymph hearts are stopped.

In birds and mammals, valves and nodes appear along the lymph channels, and movement of the extravascular fluid is accomplished by muscle action, massage, gravity, and arterial pulsations transmitted to the lymph vessels. Diffusion of molecules the size of albumin or smaller have a part in this process. Most of the disorders of the lymphatic system begin with stagnation of extravascular fluid (tissue fluid).

Certain anlages tend to carry with them to maturity some of their more important collateral systems. This is noted particularly in the nerve supply of the muscles derived from the branchial arches. The trigeminal nerve supplies the muscles derived from the first branchial arch, the facial nerve supplies the muscles derived from the second branchial arch, while the glossopharyngeal and the vagus nerves innervate those derived from the third and fourth branchial arches. The tensor tympani muscle is derived from the first arch and is innervated by the trigeminal nerve, while the near-by stapedius muscle is derived from the second arch and is supplied by the facial nerve.[3]

The best example of this developmental principle found in the lymphatic system is in the structures derived from the first branchial pouch. The first branchial pouch is the anlage for the tympanum, eustachian tube, nasopharynx, nasal cavities, and sinuses. This anlage carries its own lymphatic system in that the lymph from all of these structures drains into the retropharyngeal nodes and, to a questionable extent, into the subdigastric nodes (primary echelon)[4]. These structures are enclosed in bone, so the lymph channels through these nodes are the only exits for the lymph from these parts. This

structural arrangement increases the susceptibility of this system to difficulties resulting from lymphatic blockage.

The lymphatic bed consists of the intercellular and interstitial spaces and lymph pathways in the mucosa of the sinuses, nasal cavities, adenoid, eustachian tube, and middle ear. For the purposes of this discussion, consideration will be given particularly to the characteristics of the lymph bed in the sinuses; for, with the possible exception of the adenoid, the sinuses are the most frequent site of infection which affects the retropharyngeal lymphatic system. Because of its more frequent involvement and accessibility, particular consideration will be directed to the maxillary sinus. To understand better the formation of abnormal amounts of tissue fluid the variables which affect its production and removal will be considered briefly.

FUNDAMENTAL PHYSIOLOGY

Arterial capillary filtration increases with inflammation, irritation, exposure to cold, and lowered colloidal osmotic pressure of the blood (hypoproteinemia). The arterial capillary filters water and protein. The salts perfuse freely. Arterial capillary pressure is lowered and filtration is reduced by dilatation of the arteriovenous anastomoses. Venous capillary absorption is limited to water, salts, and certain diffusable products. Absorption is retarded by an increase in venous pressure (passive congestion). Absorption is accelerated by increased tissue pressure and lowered venous pressure (elevation of the part and physical pressure.) Tissue pressure is gauged by the resistance a tissue offers to dilatation of its interstitial spaces by edema fluid. It becomes greater as the rate of dilatation increases and becomes less as the tissue loses its elasticity. According to its magnitude, tissue pressure offers resistance to capillary filtration, promotes capillary absorption and lymph flow, and affects the process of molecular diffusion. The integument covering the part and the fascial planes of the body resist an increase in tissue pressure. Tissue pressure increases as the interstitial spaces lose their elasticity by becoming filled with proliferating fibroblasts.

Lymph flows normally by muscle contraction, active and passive motion, massage, and gravity. During pathologic states, due to immobility of the part, lymph flow is chiefly by gravity, tissue pressure, and pulsations transmitted from the dilated arteriovenous anastomoses to the lymph vessels by hydrostatic pressure. The lymphatic system carries the following from the tissues: protein, cellular detritus, products of cell metabolism, bacterial products, particulate matter, and little water. Acute lymphatic blockage results from the deposit of fibrin, cells, etc., in the interstitial lymph spaces, channels, and nodes (infection and malignancy). Chronic lymphatic blockage results from fibrosis of interstitial tissue spaces, lymph pathways, and nodes due to the prolonged presence of stagnant tissue fluid and bacterial products, parasites, or long-continued absorption of particulate matter (interstitial fibrosis, filariasis, pneumonoconiosis). Stagnant tissue fluid renders a part very susceptible to recurrent infection.[5]

PHYSIOLOGY OF THE SINUS MUCOSA

The ciliated epithelium and mucus covering of the normal sinus mucosa carries out the physiology of the normal sinus by keeping the lining membrane free from extraneous material. This mucosa is composed normally of a single or stratified layer of ciliated columnar cells frequently lacking a well-defined basement membrane. The stroma of the normal mucosa is often not more than 0.02 mm. in thickness and is composed of loosely spaced fibroblasts with interstitial spaces which are capable of rapid wide distention by edema fluid.[6] This means that the tissue pressure is low and there is little resistance to filtration resulting from increased capillary permeability. Near the ostium the mucosa is thicker and glands are more numerous. This indicates that the resistance to edema formation is greater near the ostium, leaving this area open for drainage. Gravity apparently plays an important part in the physiology of the sinus mucosa. As edema fluid dilates the interstitial spaces of the mucosa, it is free fluid and not a part of the tissue gel, i.e., it may be aspirated with a needle and is free to gravitate and render most edematous the most dependent part of the sinus mucosa. This gravitational effect is particularly noticeable post mortem in the edema of the sinus mucosa which occurs as a part of the generalized edema resulting from hypoproteinemia. Correlation of these facts explains the anatomic formation of the maxillary sinus. As the mucosa becomes edematous it increases in volume in the part of the sinus away from the ostium which results in the secretion being forced into an area adjacent to the ostium. The ability of the stroma of this mucosa to become edematous and then return to normal is a criterion of its physiologic efficiency and its complete recovery from infection or irritation.[7, 8]

The normal sinus mucous membrane is a nonabsorbing structure except in that it is permeable to substances which gain entrance by molecular diffusion. Dyes, particulate matter, etc., when placed in the normal sinus are always carried away through the ostium on its mucus covering unless some of their component molecules diffuse into the mucosa, or some irritation produces an edema which opens the avenues of lymphatic absorption.

FUNCTIONAL PATHOLOGY OF THE SINUS MUCOSA

The increased capillary permeability and filtration resulting from irritation or infection of the mucosa results in dilatation of the interstitial spaces of the mucosa. The amount of edema and swelling of the mucosa and the amount of protein filtered through the capillary is proportional to the severity of the stimulus. Since all air-containing cavities of the body tend to lose their air when they become infected, the edematous increase in volume of the mucosa and the secretion in the sinus should, when necessary, be able to fill entirely the cavity of the sinus. This filling of the sinus cavity with edematous membrane and secretion drives air from the cavity, raises the tissue pressure, and, since the cavity is enclosed by rigid walls, allows lymph to be pumped from the part by pulsations transmitted to the lymph vessels from the dilated arteriovenous

anastomoses by hydrostatic pressure. This explains the tendency of large sinuses to develop chronic infection. Their size may be so great that the secretion and swelling of the mucosa cannot approximate the volume of the sinus. This leads to air cavitation and tissue fluid stagnation in the sinus mucosa.

Fibroblasts, when given a normal amount of food (protein), will not proliferate. When bathed in tissue fluid of high protein content for a period of time, they proliferate and fill the dilated tissue spaces in order to drive from the area products of cell metabolism, cellular detritus, bacterial products, et cetera. This proliferation results in permanent fibrous overgrowth of the part and loss of tissue elasticity.[9]

When the sinus mucosa becomes fibrotic following tissue fluid stagnation it cannot become edematous and approximate the capacity of the sinus and thereby raise its tissue pressure by impinging upon the rigid walls of the sinus. The only increase in tissue pressure of which the fibrotic mucosa is capable is derived from its increased density. This, however, is ineffective because the tissue has lost the normal elastic mobility of its interstitial spaces and the fibrosis prevents the normal dilatation of the blood vessels which accompanies inflammation. When the fibrosis becomes extensive, particularly when it involves the region of the ostium, the blood supply to the glands is reduced, the glands atrophy, and the mucus secretion is diminished or absent. This terminates in air cavitation and inability of the arteriovenous anastomoses to transmit their pulsations to the lymph vessels by hydrostatic pressure with resulting lymph stasis. As water is absorbed from stagnant tissue fluid by the venous capillaries there is an increase in protein concentration and a rise in colloidal osmotic pressure of the stagnant tissue fluid. The foregoing principles of physiology and functional pathology will be applied to the following types of sinusitis.

ACUTE BACTERIAL SINUSITIS

Bacterial infection of the sinus mucosa may occur on its surface or in its tissue spaces when they become dilated by edema fluid. During the usual acute purulent sinusitis the mucosa of the sinus becomes edematous and the remaining air cavity is filled with secretion. During virulent infection of a previously normal mucosa the volume of the mucosa gradually increases until it approximates the capacity of the sinus, and the volume of the secretion becomes constantly less until it is absent or negligible. When this cycle has been completed the sinus may be considered healed except for the return of its mucosa to normal thickness, which ordinarily occurs rapidly. Variations of this clinical picture occur frequently as the result of invasion by bacteria of attenuated virulence, immunologic reactions, antibiotics, treatment, et cetera.

CHRONIC BACTERIAL SINUSITIS

This is usually caused by proteinized edema fluid of the acute stage remaining in the dilated tissue spaces of the mucosa. This leads to proliferation of the fibroblasts of the stroma and a permanent uniform thickening and over-

growth of the part. The result is a mucosa which can no longer become edematous and carry out its physiologic function of approaching the capacity of the sinus and returning to normal. This frequently terminates in a sinus which is unable to empty itself of contained secretion. This type of sinus infection may be relieved by irrigation, but there will be a recurrence of retention of secretion following certain respiratory infections. Fibrosis of the mucosa usually produces complete local lymphatic blockage so that there is no systemic absorption through the lymphatic system and no intranasal tissue turgescence to betray the presence of the pus in the sinus. This absence of intranasal tissue turgescence is evidence that there is little in the lymph bed to be removed by the lymph pump mechanism or, if stagnant tissue fluid is present in the lymph bed, it has been walled off in the interstitial spaces by fibrosis. This fibrosis delays greatly or absolutely prevents the absorption of dye injected into the sinus. The proclivity of lymph channels for rapid regeneration may allow a fibrotic mucosa to resume some of its former physiologic characteristics, if it is kept free of infection for a period of time.

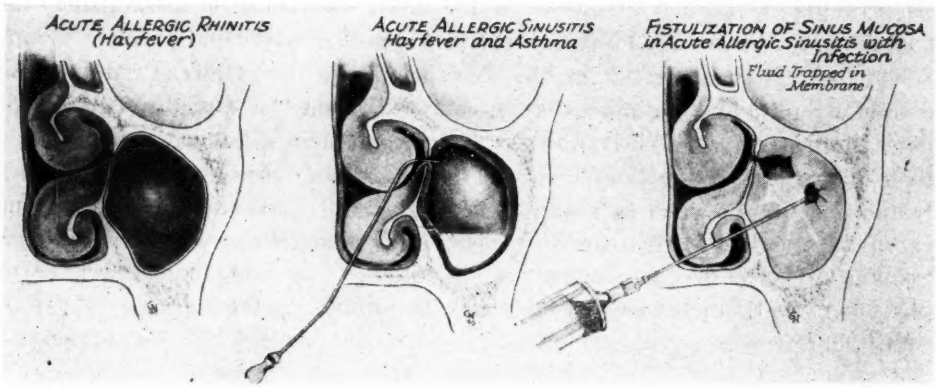

Fig. 1.—Drawings showing the transition of acute allergic rhinitis into acute allergic sinusitis. During seasonal hay fever patients suffer from alternating nasal stenosis due to increased turgescence of their intranasal tissues. Their nasal stenosis varies directly with the concentration of allergen in the air and subsides promptly as the allergen disappears. Patients with acute allergic sinusitis usually consult the rhinologist during or soon after the hay fever season complaining of complete nasal stenosis or asthma or both. Excessive intranasal tissue turgescence is a constant finding in these patients and often has been intensified by excessive intranasal medication. Irrigation of the maxillary sinus through the natural ostium will relieve these patients of their nasal stenosis and asthma if the sinusitis is mild. If severe, and tissue fluid has become trapped in the sinus mucosa, irrigation of the sinus and fistulization of the sinus mucosa by sinus puncture definitely accelerates their recovery. The secretion recovered from the sinuses is usually white, mucoid, and of low protein content with low colloidal osmotic pressure. Clinical experience leaves no doubt that absorption of components of the secretion or trapped tissue fluid is an etiological factor in their constant nasal stenosis and asthma. Bacteria may or may not be demonstrable.

ALLERGIC MAXILLARY SINUSITIS

This type of sinusitis may be divided into three stages, each of which may be progressive.

1. *Acute allergic sinusitis* ordinarily accompanies or follows hay fever. In this stage there may be slight or marked edema of the sinus mucosa. Complete nasal stenosis due to swelling of the turbinates is frequently present. This intranasal tissue turgescence is the effort of the lymph pump mechanism to re-

move an irritant from the lymph bed. The secretion found in the maxillary sinus is usually white, mucoid, and of small amount. Its total protein content is low, and, since the allergen is nonbacterial, these patients rarely have lymphatic blockage. The open lymphatic system allows the albumin to diffuse out leaving a relatively high percentage of globulin. The colloidal osmotic pressure of the secretion is very low and no doubt the absorption of components of the material in the sinus cavity is responsible for the bronchial asthma which is often an accompanying constitutional symptom. Irrigation of the maxillary sinus will frequently relieve these patients of their nasal and asthmatic symptoms until they receive a new dose of allergen. At times particulate matter is found in the washings. If the mucosa has become very edematous, often it is advisable to produce fistulization of the mucosa by sinus puncture. Fistulization allows the tissue fluid trapped in the mucosa to drain into the sinus and definitely hastens recovery.

2. *Subacute allergic sinusitis* follows the acute stage when bacteria, bacterial products, or a potent allergen gains entrance to the open tissue spaces of the mucosa. When this occurs a true lymphangitis develops which is characterized by marked edema of the mucosa of the sinus. The secretion is often scanty and the mucosa may be so edematous that it fills the sinus cavity. Many of these patients have asthmatic attacks early in the progress of the disease and later many of them have asthma constantly. Apparently the severity of their asthma is related to the virulence of the bacterial infection or the amount of allergen fixation present in the sinus mucosa. This condition is always bilateral and in its more acute form is associated with a marked constant increase in intranasal tissue turgescence. While lymphangitis of the mucosa is present, systemic complications such as pleurisy, pneumonitis, nephritis, and arthritis, are likely to occur if extensive surgery is instituted. The frequency and severity of the patient's asthmatic symptoms are fair criteria of the amount of surgery that may be safely employed. If the asthmatic attacks are intermittent and fairly mild with normal temperature, low white blood cell count, and comparative freedom from râles, minor surgical procedures may be instituted with safety. However, if there are severe continuous asthmatic symptoms with anoxemia and other acute symptoms such as increased white cell count, considerable purulent secretion in the sinuses, and many râles, the treatment should be conservative until the condition improves. This subacute stage, with or without regressive intervals, may last for years. Since these patients have relatively large amounts of stagnant tissue fluid in their sinus mucosa they are particularly susceptible to recurrent bacterial infection with exacerbation of their asthmatic and nasal symptoms.

The secretion from the sinuses in these patients conforms to that found in purulent sinusitis except that the globulin is in relatively greater concentration because the lymphatic system usually is open and the albumin can be carried away by diffusion. The absorption of globulin, one of its catabolic products, or some substance fixed to it may be one cause of bronchial asthma. Since it has been impossible so far to isolate and deal with the exact molecule

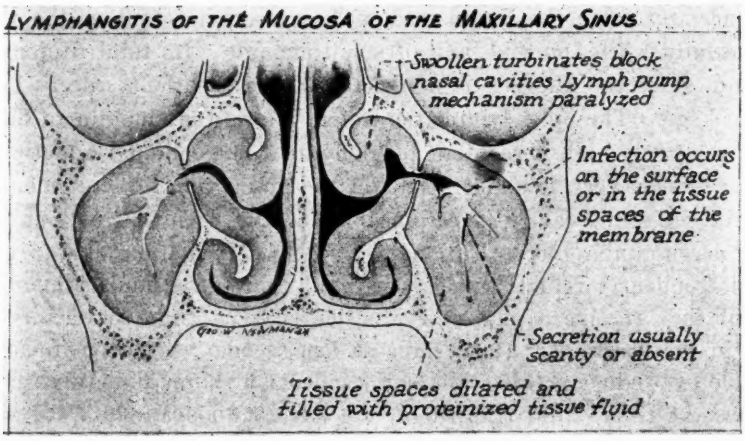
LYMPHANGITIS OF THE MUCOSA OF THE MAXILLARY SINUS
Swollen turbinates block nasal cavities lymph pump mechanism paralyzed
Infection occurs on the surface or in the tissue spaces of the membrane
Secretion usually scanty or absent
Tissue spaces dilated and filled with proteinized tissue fluid

Fig. 2.—Drawing showing subacute allergic sinusitis with stagnation of tissue fluid in the sinus mucosa. This condition is always bilateral and pathologically is a true subacute lymphangitis of the mucosa of the sinuses. It follows acute allergic sinusitis when tissue fluid has been trapped and is allowed to remain in the sinus mucosa. These patients have swollen turbinates, often have nasal intonation of the voice, and frequently state that "once you have sinus trouble you always have sinus trouble." Stagnation of tissue fluid in the mucosa may continue for years, renders the individual very susceptible to recurrent sinus infection and often is associated with recurrent attacks of bronchial asthma. Their nasal stenosis and asthma may disappear following application of local pressure to the mucosa of their maxillary sinuses. If acute asthmatic or infection symptoms are present, systemic complications such as pleurisy and pneumonitis are prone to occur following traumatism to this edematous mucosa.

Fig. 3.—Photomicrograph of area of dilated tissue spaces in the maxillary sinus mucosa of patient with subacute allergic sinusitis. The only pathology presented by this mucosa consists of slight increase in white blood cells, dilated tissue spaces containing excessive tissue fluid, and, in the lower right, areas of newly formed fibrous tissue. Local pressure is more effective if applied to this type of mucosa before the areas of newly formed fibroblasts appear. Clinical observations of the relation of the volume of this mucosa to the capacity of the sinus reveal three pathologic states. (1) During the early edematous stage the mucosa may approximate the capacity of the sinus. (2) As fibroblasts proliferate and contract, the volume of the mucosa shrinks and may remain in this redundant form for years. (3) As polypi form, the volume of the mucosa again may approximate or fill the capacity of the sinus. (Magnification ×75.)

which is responsible for chronic infectional or allergic edema of the sinus mucosa, the logical therapeutic procedure is to institute measures which would help remove the offending agent. The use of local pressure for this purpose will be described briefly.[10]

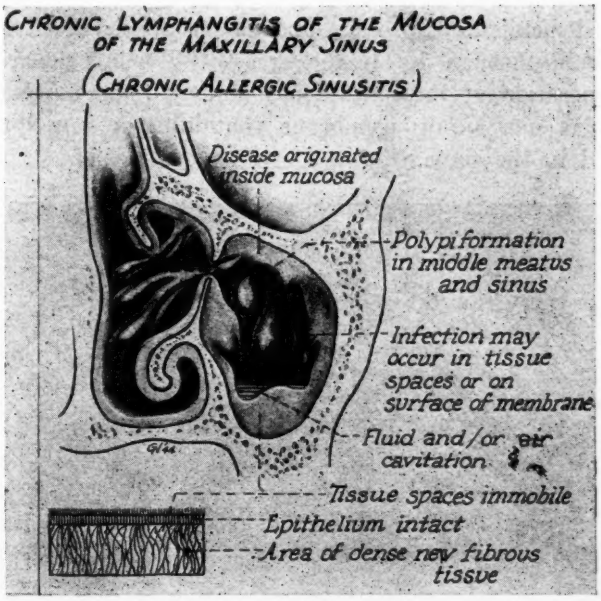
CHRONIC LYMPHANGITIS OF THE MUCOSA OF THE MAXILLARY SINUS
(CHRONIC ALLERGIC SINUSITIS)
Disease originated inside mucosa
Polypi formation in middle meatus and sinus
Infection may occur in tissue spaces or on surface of membrane
Fluid and/or air cavitation
Tissue spaces immobile
Epithelium intact
Area of dense new fibrous tissue

Fig. 4.—Drawing showing chronic allergic sinusitis which is a true chronic lymphangitis of the mucosa of the maxillary sinus. This condition is the terminal result of long-continued retention of excessive tissue fluid in the interstitial spaces of the mucosa. When infection occurs following the formation of alternating areas of fibrosis and dilated tissue spaces in the mucosa, the rise in tissue pressure produces polypoid formations from the areas of dilated tissue spaces. After chronic infection, extensive polypoid degeneration and fibrosis have occurred in the mucosa of the sinus, the mucosa should be removed so a new lining membrane containing a new lymphatic system can be formed.

3. *Chronic allergic sinusitis* pathologically follows the subacute stage when the increased content of protein and bacterial products present in the interstitial spaces of the mucosa promotes the growth of fibroblasts. The dilated tissue spaces become filled with fibroblasts which contract and reduce the volume of the edematous mucosa. The fibrosis which follows strictly purulent infection of the mucosa is uniform. Fibrosis of the mucosa in the chronic stage of allergic disease is characterized by the formation of alternating areas of fibrosis and dilated tissue spaces. As repeated infection of the mucosa occurs and the intramucosal tissue pressure rises, polypi formations protrude from the areas of dilated tissue spaces. The stroma of the mucosa of the middle meatus is normally possessed of areas of loosely spaced fibroblasts. Through these areas flows all of the lymph from the anterior group of sinuses. As lymphatic blockage due to cellular infiltration and fibrosis occurs in the interstitial spaces and lymph channels following prolonged infection, the tissue pressure rises in the sinus mucosa and hydrostatic pressure forces polypi to protrude from the areas of dilated lymph spaces in the mucosa of middle

meatus. Although polypi may form from the mucosa of the maxillary sinus and prolapse through its ostium, the most frequent cause of polypi formation from the mucosa of the middle meatus is extension of the process of fibrosis from the mucosa of the maxillary sinus to the lymph pathways of the middle meatus. This fibrosis is due to the draining of abnormal amounts of the products of cell metabolism, protein, and bacterial products from the anterior group of sinuses through its lymph spaces. When extensive fibrosis and polypoid degeneration of the mucosa has occurred, the mucosa should be removed so that a new lining membrane containing a new lymphatic system may be formed in the sinus.

Fig. 5.—Photomicrograph showing a lake of tissue fluid in the mucosa of a boy, 14 years of age, who was suffering from chronic allergic sinusitis. Following prolonged tissue fluid stagnation, as the tissue loses its elasticity the interstitial tissue spaces are disrupted by gravitation of tissue fluid which collects in puddles comparable to pond formation in a marsh. This occurs most frequently near the tip of pedunculated polypi and in sessile polypi in the inferior part of the maxillary sinus. In certain instances this fluid may be aspirated after needle puncture, and at times bacteria may be demonstrated in it. (Magnification ×50.)

PRESSURE RATIONALE

The physiology of the body is closely governed by the permeability of the natural membranes. The variables of membrane permeability as they affect osmotic pressure and molecular diffusion are (1) time, (2) membrane area, (3) concentration difference across the membrane, (4) size and shape of the diffusing molecules, (5) temperature, and (6) pressure.[11]

Of these variables, local pressure can best be utilized to accelerate removal of tissue fluid and promote molecular diffusion. The application of local pres-

sure to the mucosa of the maxillary sinus is designed to replace the air in the cavity of the sinus with a fluid medium through which arterial pulsations can be transmitted to the tissue spaces and lymph channels by hydrostatic pressure. As the tissue pressure is increased, the water and salts are absorbed from the tissue fluid by the venous capillaries and the process of diffusion of molecules of bacterial, body cell, and allergen products through the lymphatic system is accelerated. This process occurs normally during acute inflammation of the previously normal mucosa—the mucosa becomes markedly edematous, approximates the capacity of the sinus, and increases its tissue pressure. After varying periods of time, depending upon the frequency and severity of the instances of increased tissue pressure during subacute allergic sinusitis, polyps may approach or entirely fill the capacity of the sinus. This formation of polypoid masses is nature's effort to raise the intrasinus pressure by driving air from the cavity with a medium through which hydrostatic pressure may be utilized to transmit arterial pulsations to the tissue spaces and lymph channels. Nature's attempt to relieve tissue fluid stagnation by polypi forma-

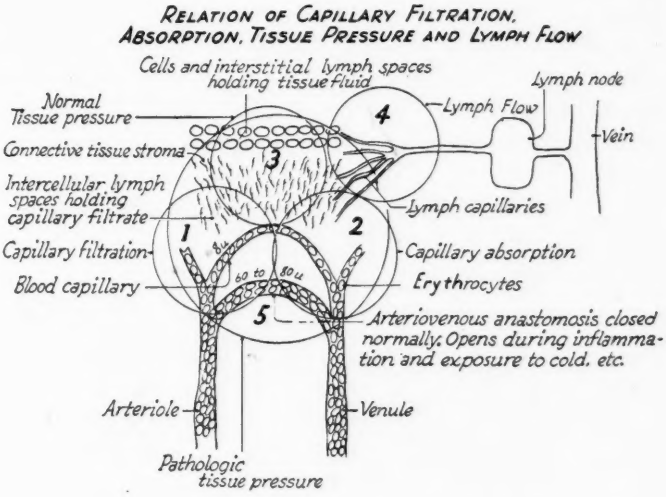

Fig. 6.—Diagram of the relation of capillary filtration, absorption, and lymph flow to normal and pathologic tissue pressure. The diagram shows four small circles and one large circle, the latter encompassing a part of each of the four small circles and the open arteriovenous anastomosis. Small Circle *1* represents arterial capillary filtration which is controlled by the colloidal osmotic pressure of the plasma, the permeability of the capillary membrane, the arterial blood pressure, and the tissue pressure. It filters water, salts, and protein. Small Circle *2* represents venous capillary absorption which is controlled by the colloidal osmotic pressure of the plasma, the permeability of the capillary membrane, the venous blood pressure, and the tissue pressure. It absorbs water, salts, and certain diffusable toxic products, but no protein. Small Circle *3* represents the normal tissue pressure which is gauged by the resistance the tissue offers to dilatation of its interstitial spaces by edema fluid. It is proportional to the density and elasticity of the tissue. According to its magnitude, it offers resistance to arterial capillary filtration and promotes venous capillary absorption and lymph flow. Small Circle *4* represents lymph flow, which is accelerated by active and passive motion of the part, massage, gravity, pulsations transmitted from the blood vessels to the lymph pathways, and increased tissue pressure. Large Circle *5* represents increased or functionally pathologic tissue pressure. It overlaps each of the smaller circles and includes the dilated arteriovenus anastomosis. Increased tissue pressure reduces arterial capillary filtration, promotes venous capillary absorption, and accelerates lymph flow by transmitting pulsations from the dilated arteriovenous anastomoses to the lymph vessels. Increase in tissue pressure is resisted by the fascial planes of the body and the integument covering the part. Following prolonged edema, tissue loses its elasticity which results in lowering of tissue pressure. Tissue pressure may be raised by application of pressure to the surface of the part.

tion would make it seem logical to place an artificial polypus in the cavity of the maxillary sinus during the early stages of edema before the mucosa has suffered from the marked fibrosis and permanent thickening incident to long-continued chronic inflammation and tissue fluid stagnation.

Up to the present time, the application of pressure to the sinus mucosa has been used only in the subacute stage of allergic sinusitis. It is not offered as a substitute for any standard practice. Immediately after the application of local pressure these patients' asthmatic symptoms may become aggravated for twenty-four to forty-eight hours, after which they may subside or entirely disappear. They often lose their slightly cyanotic appearance, enjoy free nasal respiration, and are able to indulge in more strenuous physical effort. The asthma-free duration is not known but should continue until the patient is attacked again by an allergen or bacteria. The closest cooperation between the allergist, internist, and otolaryngologist is advisable in treating these patients.

The utilization of an artificial polypus for this purpose follows:

A relatively small opening is made through the nasoantral wall under the inferior turbinate. Through this opening a No. 16 self-retaining soft rubber catheter is inserted. If there is any question about the patient having acute symptoms, this catheter should not be inserted at the time the nasoantral window is made, for the reaction it causes may seriously aggravate the symptoms. However, its use definitely aids in keeping the fenestra patent. When

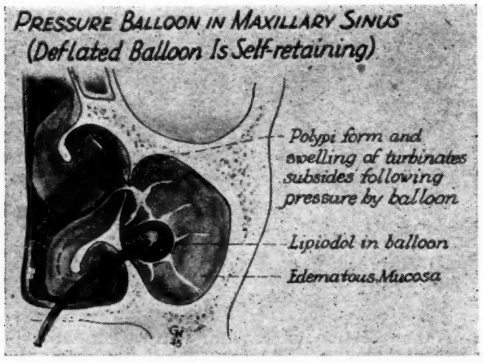
PRESSURE BALLOON IN MAXILLARY SINUS
(Deflated Balloon Is Self-retaining)
Polypi form and swelling of turbinates subsides following pressure by balloon
Lipiodol in balloon
Edematous Mucosa

Fig. 7.—Drawing showing pressure balloon used as an artificial polypus in the maxillary sinus. This appliance is designed to increase the tissue pressure of the sinus mucosa thereby promoting absorption of, and accelerating molecular diffusion in, stagnant tissue fluid. Stagnation of tissue fluid in the maxillary sinus mucosa is manifested intranasally by chronic increased turgescence of turbinate tissue. After the intrasinus pressure has been raised for a varying period of time the turbinate turgescence subsides and newly formed polypi may appear in the middle meatus, as shown by the dotted lines. Although the use of local pressure to the mucosa of the maxillary sinus was devised primarily to accelerate removal of stagnant tissue fluid its use has revealed that certain patients having stagnant tissue fluid and bronchial asthma are relieved of their asthma following application of pressure. The use of this pressure balloon should not be construed as a "cure" for all types of asthma and sinus infection. Many patients suffering from these afflictions have irreversible structural changes in their sinuses and lungs which cannot be returned to normal by pressure applied to the mucosa of their sinuses. However, the observation that certain patients are relieved of their asthma and bronchitis, regain some of the physiologic functions of their sinus mucosa and increase their sense of well-being following the application of pressure, is in accord with the experience of otolaryngologists who have observed for many years that certain patients suffering from coexisting asthma and sinus pathology are relieved of their asthma by operations which remove the diseased mucous membrane from the sinuses. The relief of symptoms following the application of pressure is additional evidence that the sinuses may be the source of some noxious substance which is an etiological factor in asthma.

this catheter has been in place long enough for the postoperative reaction to subside, usually one or two weeks, it is removed and replaced with a No. 12 self-retaining catheter which has had its bullous end enclosed in a small distensible natural rubber balloon. The catheter is cut off so that its intranasal end rides comfortably and unseen in the vestibule of the nose. The balloon is then or later inflated with lipiodol until patient feels a slight sensation of pressure in the maxillary sinus. The end of the catheter in the vestibule is tied with No. 7 braided silk cord, care being taken to tie the knot on the side of the catheter away from the nasal septum. The balloon is, if possible, further distended with lipiodol at weekly intervals and, if well tolerated by the patient, may be left in place for a protracted time (eight to twelve weeks). As the tissue pressure in the sinus mucosa is increased for a few weeks by expansion of the balloon, newly formed polypi frequently appear from the dilated tissue spaces of the middle meatus. Small granulomata, which form around the tube in the inferior meatus and polypi which form in the middle meatus may be removed after the balloon is removed.

Lipiodol is used because the progress of distention may be observed by x-ray. Also, its specific gravity (1.35), being higher than that of blood plasma (1.027), allows it to displace the sinus secretion. Most of the difficulty patients experience with this treatment arises from irritation of the septum and the tip of the nasal vestibule by the nasal end of the catheter. This irritation may be

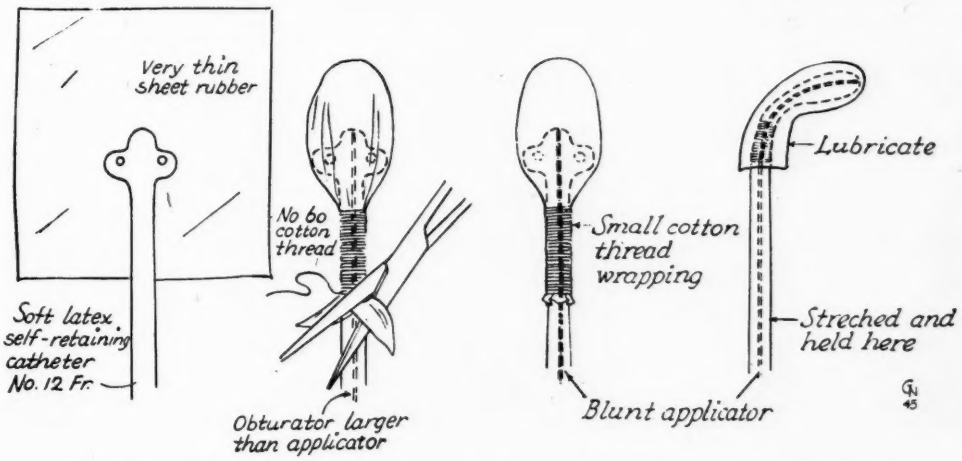

Fig. 8.—Drawings showing construction of pressure balloon used as an artificial polypus in the maxillary sinus. Materials necessary are: piece of very thin sheet rubber 3 inches square, No. 12 Fr. soft latex self-retaining catheter, No. 60 white cotton thread, curved blunt smooth throat applicator, jelly lubricant, and straight obturator. (The latter may be the shaft of a laryngeal mirror with detachable handle.) The obturator is lubricated and passed through the catheter into its retaining head. The sheet rubber is draped about the head of the catheter leaving a balloon around it about ¾ to 1½ inches in diameter. The sheet rubber is then wrapped around the neck of the catheter for about ½ inch with three layers of cotton thread, care being taken not to wrap too tightly against the obturator. Knots should be tied at several places along the wrapping. The excess rubber sheeting is cut away and the balloon is tested with air and pulled tightly against the head of the catheter. The curved applicator is lubricated and inserted. The catheter is stretched and the balloon is lubricated. It is then ready for insertion through the nasoantral opening into the maxillary sinus. This appliance may be sterilized by boiling. The cotton thread has shown no tendency to lose its efficiency after being in the sinus for three months. To remove: The balloon is deflated of lipiodol by cutting the string around the intranasal end of the catheter. Traction is made on the catheter until the wrapped portion appears under the inferior turbinate. This part of the balloon is then grasped with a small hemostat and removed by traction. This appliance should be available commercially in the near future.

minimized by using only the soft latex type of catheter in preference to the harder red rubber variety. The application of too much pressure should be avoided. The object in using this artificial polypus is not to drive the edema fluid from the mucosa by force, but rather to provide a fluid incompressible medium through which the pulsations of the arteriovenous anastomoses may be transmitted to the tissue spaces and lymph channels and thus facilitate molecular diffusion and lymph flow, thereby transforming stagnant into changing tissue

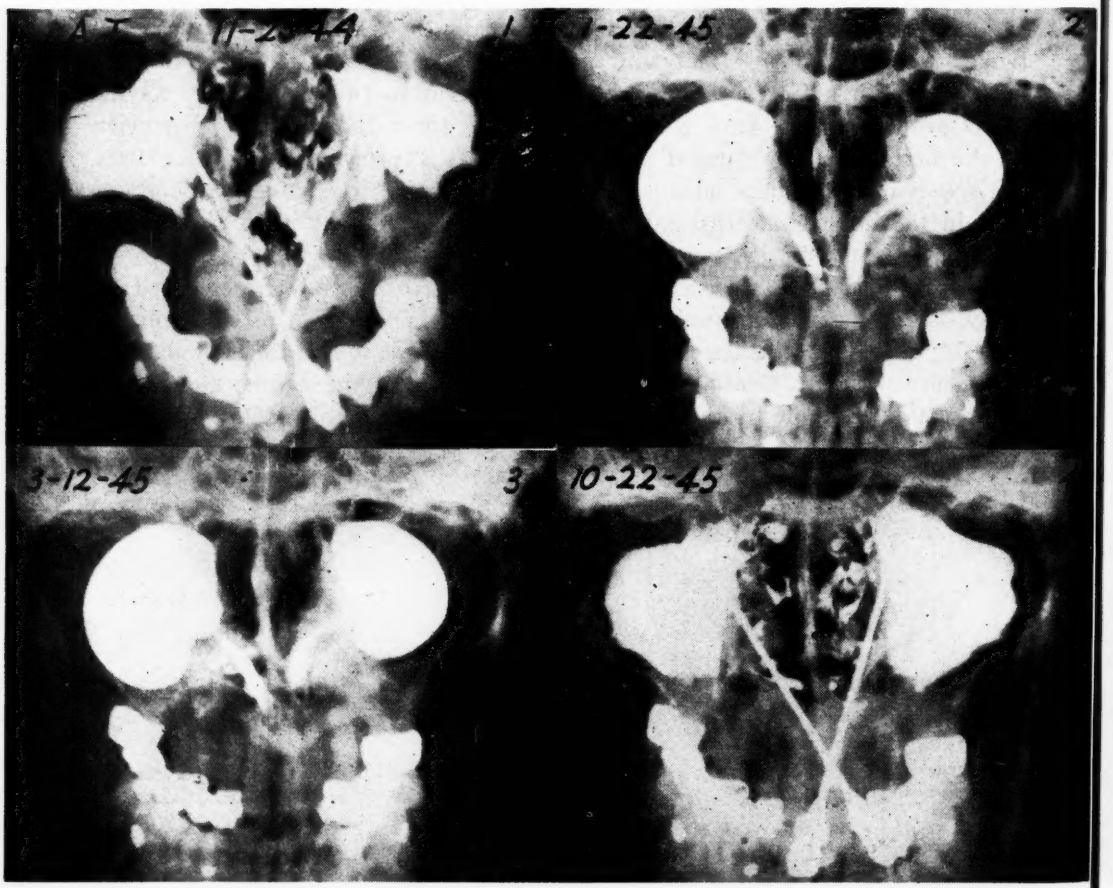

Fig. 9.—This patient, aged 55 years, had an allergic history of fourteen years' duration and allergic sinusitis. He had frequent attacks of bronchitis, nasal stenosis, and bronchial asthma. The latter had become increasingly frequent and severe. On first examination, he had small polypi in his middle meatuses, bilateral thickening of the maxillary sinus mucosa (Radiograph *1*), and asthma of two months' duration for which he had been treated by a competent allergist. Puncture and irrigation of his maxillary sinuses evacuated mucopurulent secretion. The small polypi were removed, nasoantral windows were made, and his sinuses were irrigated for two months without relief from his sinus and asthmatic symptoms. Balloons were inserted into his maxillary sinuses and inflated with lipiodol (Radiographs *3* and *4*). He was relieved of his bronchitis, nasal stenosis and asthma and gained 10 pounds weight. Pressure was continued in his sinuses for about three months. During this period large newly formed polypi appeared in his middle meatuses. After the balloons were removed from his sinuses large amounts of thick mucus secretion were evacuated by irrigation for about one month, probably indicating improvement in nutrition of glands in the mucous membrane. He was symptom-free for about seven months, then he "took cold," during a change in weather and developed bronchitis, nasal stenosis, and asthma for three days which was so mild that medication was unnecessary. His sinuses were irrigated at this time and a small amount of secretion was evacuated (Radiograph *4*). One month later, although he was entirely free of symptoms, the balloons were reinserted and will be left in place for another period to avoid tissue fluid stagnation.

fluid. As the pressure in the sinus is increased, the nasal end of the catheter will tend to protrude toward the tip of the nasal vestibule. After each injection, part of the catheter should be cut off if it touches the tip of the vestibule.

SUMMARY

1. The lymphatic system arises in the phylogenetic scale of life as it becomes necessary to remove from the body substances not readily absorbed by the blood. Its primary function is removal of components of extravascular fluid in the lymph bed. Alterations of this activity, usually produced by some type of lymphatic blockage or lowered tissue pressure, lead to stagnation of fluid in the interstitial tissue spaces.

2. Tissue fluid stagnation in the lymph bed of the mucosa of the paranasal sinuses plays a part in the pathogenesis of allergic sinusitis.

3. Irrigation of the maxillary sinus and fistulization of the sinus mucosa by sinus puncture to relieve trapped tissue fluid are efficient therapeutic measures in severe acute allergic sinusitis.

4. The removal of excess tissue fluid from the edematous mucosa of the maxillary sinus may be accelerated by application of local pressure to the mucosa. The formation of polypi in the middle meatus due to this increased tissue pressure in the mucosa of the maxillary sinus is described.

5. The application of pressure to the edematous mucosa of the maxillary sinus during subacute allergic sinusitis is an aid in relieving some cases of bronchial asthma. The duration of this relief is variable. So far it has continued until the patient is attacked again by an allergen or bacteria. The exact criteria for selecting patients suitable for the application of pressure to their maxillary sinuses are not well established. Apparently pressure should be applied as soon as the definite diagnosis of tissue fluid stagnation in the mucosa is made. Often this is possible long before constitutional symptoms such as bronchial asthma appear. The application of pressure to the mucosa of the maxillary sinus has a good physiologic background. Its therapeutic and practical clinical results can be evaluated better after it has been used more extensively.

The works of Dr. Cecil K. Drinker, professor of physiology at Harvard University, have been quoted freely.

I am indebted to Mr. George A. Neuman and his staff of the department of medical illustrations for their excellent technical aid.

REFERENCES

1. Drinker, C. K., and Yoffey, J. M.: Lymphatics, Lymph and Lymphoid Tissue, Cambridge, Mass., 1941, Harvard University Press, pp. 4, 26, 53, 55, 58, 80, 83, 189-190, 284, 286, 290, 291, 293, 300, 301, 305, and 307-309.
2. Cowdry, E. V., editor: Human Biology and Racial Welfare, New York, 1930, Paul B. Hoeber, Inc., p. 38.
3. Arey, L. B.: Developmental Anatomy, ed. 4, Philadelphia, 1940, W. B. Saunders Company, pp. 465, 467, and 501.
4. Rouviere, H.: Anatomy of the Human Lymphatic System, Translated by M. J. Tobias, Ann Arbor, 1938, Edwards Brothers, Inc.

5. Drinker, C. K., Field, M. E., Ward, H. K., and Lyons, C.: Increased Susceptibility to Local Infection Following Blockage of Lymph Drainage, Am. J. Physiol. **112**: 74, 1935.
6. Piersol, G. A.: Normal Histology, ed. 2, Philadelphia, 1894, J. B. Lippincott Company, p. 403.
7. Robison, J. M.: Lymphangitis of the Mucosa of the Paranasal Sinuses, Texas State J. Med. **40**: 193, 1944.
8. Robison, J. M.: Lymphangitis of the Retropharyngeal Lymphatic System, Arch. Otolaryng. **40**: 385, 1944.
9. Drinker, C. K., Field, M. E., Heim, J. W., and Leigh, O. C., Jr.: The Composition of Edema Fluid and Lymph in Edema and Elephantiasis Resulting From Lymphatic Obstruction, Am. J. Physiol. **109**: 572, 1934.
10. Robison, J. M.: Pressure Treatment of Allergic Sinusitis. (To be published.)
11. Davson, Hugh, and Danielli, J. F.: The Permeability of Natural Membranes, New York, 1943, The Macmillan Company.

ADDITIONAL REFERENCES

1. Adolph, E. F.: Metabolism and Distribution of Water in Body and Tissues, Physiol. Rev. **13**: 336, 1933.
2. Arnold, L., Ostrom, M. L., and Singer, C.: Autosterilizing Power of the Nasal Mucous Membrane, Proc. Soc. Exper, Biol. & Med. **25**: 624, 1928.
3. Baum, H. L.: Incidence of Allergy in Rhinologic Practice, Arch. Otolaryng. **20**: 804, 1934.
4. Buhrmester, C. C.: A Study of the Hydrogen-Ion Concentration, Nitrogen Content and Viscosity of Nasal Secretions, Ann. Otol., Rhin. & Laryng. **42**: 1040, 1933.
5. Cantarow, A.: Water Balance, Edema and Dehydration, Internat. Clin. **1**: 266, 1939.
6. Childrey, J. H., and Essex, H. E.: Absorption From the Mucosa of the Frontal Sinus, Proc. Staff Meet., Mayo Clin. **6**: 345, 1931; Absorption From the Mucosa of the Frontal Sinus, Arch. Otolaryng. **14**: 564, 1931.
7. Clark, E. R., Arteriovenous Anastomoses, Physiol. Rev. **18**: 229, 1938.
8. Drinker, C. K.: The Lymphatic System: Its Part in Regulating Composition and Volume of Tissue Fluid, Lane Medical Lectures, Stanford University, California, 1942, Stanford University Press, vol. 4, pp. 66-92.
9. Drinker, C. K., Field, M. E., and Homans, J.: The Experimental Production of Edema and Elephantiasis as a Result of Lymphatic Obstruction, Am. J. Physiol. **108**: 509, 1934.
10. Drinker, C. K., Field, M. E., and White, J. C.: Lymph Pressures in Sterile Inflammation, J. Exper. Med. **56**: 363, 1932.
11. Fenton, R. A.: "Reticulo-Endothelial" Components of Accessory Sinus Mucosa: Experimental and Clinical Observations, Arch. Otolaryng. **14**: 586, 1931.
12. Fenton, R. A., and Larsell, O.: An Experimental and Clinical Study of Histiocytes in Acute and Chronic Inflammation of the Accessory Sinuses, Laryngoscope **43**: 233, 1933.
13. Fenton, R. A.: Histopathology and Clinical Interpretation of Experimental and Clinical Sinusitis, Arch. Otolaryng. **23**: 18, 1936.
14. Fenton, R. A., and Larsell, O.: The Defense Mechanisms of the Upper Respiratory Tract, Ann. Otol., Rhin. & Laryng. **46**: 306, 1937.
15. Freedman, A. O.: The Pathogenesis of Polyposis Nasi, Arch. Otolaryng. **2**: 250, 1925.
16. Gamble, J. L.: Extracellular Fluid; Renal Defense of Extracellular Fluid Control of Acid-Base Excretion and Factors of Water Expenditure (William Sydney Thayer and Susan Read Thayer Lecture), Bull. Johns Hopkins Hosp. **61**: 174, 1937.
17. Hartz, H. J.: The Lymphatics of the Nose and Nasopharynx, With Consideration of the General Lymphatic System, Tr. Am. Acad. Ophth. **16**: 119, 1911.
18. Harvey, S. C., and Howes, E. L.: Effect of High Protein Diet on the Velocity of Growth of Fibroblasts in the Healing Wound, Ann. Surg. **91**: 641, 1930.
19. Katz, G., and Cohen, S.: Experimental Evidence for Histamine Release in Allergy, Chem. Abstr. **36**: 555, 1942.
20. Katz, G.: Histamine Release in the Allergic Skin Reaction, Proc. Soc. Exper. Biol. & Med. **49**: 272, 1942.
21. Krogh, A.: The Exchange of Water Between the Blood and the Tissue Spaces, in the Anatomy and Physiology of Capillaries, ed. 2, New Haven, 1929, Yale University Press.
22. Landis, E. M., Jonas, L., Angevine, M., and Erb, W.: The Passage of Fluid and Protein Through the Human Capillary Wall During Venous Congestion, J. Clin. Investigation **11**: 717, 1932.
23. Larsell, O., and Fenton, R. A.: Further Research on Experimental and Clinical Sinusitis, Arch. Otolaryng. **20**: 782, 1934.

24. Larsell, O., and Fenton, R. A.: Lymphatic Pathways From the Nose, Arch. Otolaryng. **24**: 696, 1936.
25. Lindsay, J. R., and Walsh, T. E.: Nasal Secretions: The Value of Cytologic Examination to the Rhinologist, Arch. Otolarygn. **17**: 783, 1933.
26. Linton, C. S.: Resistance of Upper Respiratory Mucosa to Infection, Ann. Otol., Rhin. & Laryng. **42**: 64, 1933.
27. Mullin, W. V.: The Relation of Paranasal Sinus Infection to Disease of the Lower Respiratory Tract, J. A. M. A. **87**: 739, 1926.
28. McCarrell, J. D.: Lymphatic Absorption From the Nasopharynx, Am. J. Physiol. **126**: 20, 1939.
29. McMahon, B. J.: The Spread and Phagocytosis of Particulate Matter in Nasal Mucous Membrane of the Rabbit, Ann. Otol., Rhin. & Laryng. **42**: 660, 1933.
30. Nemours, P. R., and Wenner, W. F.: The Effect of Trypan Blue on Eosinophilia Experimentally Produced in the Maxillary Sinus Mucosa, Ann. Otol., Rhin. & Laryng. **40**: 852, 1931.
31. Proetz, A. W.: The Displacement Method of Sinus Diagnosis and Treatment, St. Louis, 1931, Annals Publishing Company, p. 29; Essays on the Applied Physiology of the Nose, ibid., 1941, p. 111.
32. Reichert, F. L.: The Regeneration of the Lymphatics, Arch. Surg. **13**: 871, 1926.
33. Robison, J. M.: Subacute Catarrhal Otitis Media and Mastoiditis With Effusion, South. M. J. **35**: 815, 1942.
34. Sabin, F. R.: The Origin and Development of the Lymphatic System, Baltimore, 1913, Johns Hopkins Press.
35. Starling, E. H.: On the Absorption of Fluids From the Connective Tissue Spaces, J. Physiol. **19**: 317, 1895.
36. Stevens, F. A.: Chronic Infectional Edema, J. A. M. A. **100**: 1754, 1933.
37. Thompson, W. D., Ravdin, L. S., and Frank, I. L.: Effect of Hypoproteinemia on Wound Disruption, Arch. Surg. **36**: 500, 1938.
38. Trotter, H. A.: The Surgical Anatomy of the Lymphatics of the Head and Neck, Ann. Otol., Rhin. & Laryng. **39**: 384, 1930.
39. Tweedie, A. R.: Nasal Flora and Reaction of the Nasal Mucus, J. Laryng. & Otol. **49**: 586, 1934.
40. Wenner, W. F., and Nemours, P. R.: The Mucosa of the Maxillary Sinus of the Rabbit, Arch. Otolaryng. **15**: 270, 1932.
41. Wright, J.: The Primordial Nature of the Forces Exerted Against the Penetration of Bacteria Beneath the Surface of the Body, New York State J. Med. **83**: 118, 1906.

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Original Articles

THE VOLUMETRIC INCIDENCE OF ATMOSPHERIC ALLERGENS

III. Rate of Fall of Pollen Grains in Still Air

Oren C. Durham,* North Chicago, Ill.

SERIOUS technical difficulties were encountered by Scheppegrell,[1] Cocke,[2, 3] and Dahl[4] in devising methods of determining the number of pollen grains in a cubic yard of air from the number caught on a unit area of gravity slide. Several years ago, Dahl suggested that no further progress could be made with the problem until someone should take time to determine experimentally the actual specific gravity of the pollen grains of different species, as well as their particular rates of fall in still air. Referring to the inadequate pioneer work of this sort done in Europe by Dyakowska,[5] he said: "Amplification of such studies would directly yield the velocity of fall of various kinds of grains, including those with spiny surfaces, and there would, then, be a far more adequate basis upon which to devise factors for calculating the approximate number of pollen grains per cubic yard of air." The present series of papers is the outcome of a painstaking attempt to supply that "far more adequate basis." In the first paper of this series,[9] I supplied specific gravity determinations for several species of wind-borne pollens, and in this paper I am, incidentally, adding further data of the same sort. Table I shows how my data compare with those of Pohl[6] for 10 species tested by both of us.

Table I. Specific Gravity of Pollen Grains

(A Comparison of Existing Experimental Data)

POLLEN	POHL	DURHAM
Pine	0.39	0.45
Hazelnut	1.00	1.09
Oak	1.04	1.04
Alder	0.75	0.97
Birch	0.81	0.94
Beech	0.71	0.94
Juniper	0.40	1.08
Orchard Grass	0.98	0.91
Corn	0.35	1.00
Hemp	1.09	0.82

In 1922, Bodmer[7] determined the rate of fall of pollen grains of 20 tree species using a glass tube 98 cm. long and 35 mm. in diameter. Charges of pollen were made through an opening 0.5 cm. square in the cap at the upper end. The pollen grains were caught at the lower end on glass slides changed

*From the Biological Laboratories of Abbott Laboratories.

at regular intervals. Ten years later Knoll,[8] with a similar apparatus, checked some of Bodmer's determinations and made additional ones of his own. Some four years after this, Dyakowska[5] experimented with freshly matured pollen from 18 species of trees, timing the "rapidity of falling down" of the various pollens in a tin tube 2 M. high and 120 mm. in diameter (more than 3½ times the diameter of the tubes used by Bodmer and by Knoll). The following description of the method is quoted:

"An aperture was cut out at the bottom of the tube and through it a slide was shoved in. A glass-globe was placed on the top of the tube. That part of the glass-globe which was in contact with the tube, was smeared with vaseline so as to obtain better compactness and to diminish the circulation of the air in the tube, during the time while the pollen was falling down. Thus, the possibility of carrying out the researches in more or less motionless air was obtained and this is of principal importance for the whole problem of the rapidity of the falling down.

"The researches themselves on the falling down had the following course: A more or less similar quantity of the examined pollen, was placed in the glass tube, bent at right angle. Then, it was blown in, with the aid of a small rubber pump, into the glass-globe, taken out of the tube and kept near by, on the level of the top of the tube. The globe, with the dispersed pollen, was rapidly put on the top of the tube and after 10 seconds, the first slide, smeared with glycerine-gelatine, was shoved in the aperture at the base of the tube. Subsequently, every 10 seconds the slides were changed. The numbered slides, taken out of the tube and containing the pollen grains in the gelatine, were covered with a cover glass."

PRELIMINARY EXPERIMENTS

At the outset of my investigations I was aware only of the work of Dyakowska. Consequently, I assumed that the velocity of fall should be the same for a given pollen regardless of the dimensions of the tube enclosing the column of still air. My first determinations were made with a glass tube 76 mm. in diameter. This apparatus yielded a rate of fall for ragwed pollen which was much greater than the theoretical rate. In seeking the cause of the difficulty I found that the length of the air column was of no consequence, but that air chambers made of different materials and particularly those of different caliber gave widely varying rates of fall for ragweed pollen. Consequently considerable time was spent in selecting a suitable air chamber.

Glass, paper, and iron tubes of different calibers were tried. Table II shows that in glass as well as in iron tubes the rate of fall for ragweed pollen varies directly with the diameter of the chamber; the largest tube of a given material gives the highest rate of fall and the smallest tube gives the slowest rate. These differences I attributed to two possible factors, convection currents within the air chamber and static charges either on the pollen grains themselves, or on the walls of the chamber, or on both. Every effort was made to avoid thermal effects in the air column. The work was carried on in a quiet, unventilated, and unheated inner room. When enough time was allowed for

TABLE II. AVERAGE RATE OF FALL OF RAGWEED POLLEN GRAINS IN STILL AIR
(Common Ragweed [Lot A]; Diameter, 20 Microns)

MATERIAL	DIAMETER OF CHAMBER (MM.)	AVERAGE RATE OF FALL (FT. PER SEC.)
Glass (coated inside with petrolatum)	33	0.036
Glass (coated inside with petrolatum)	47	0.047
Glass (coated inside with petrolatum)	76	0.068
Cardboard (dry)	60	0.062
Cardboard (coated inside with petrolatum)	60	0.056
Iron	51	0.029
Sheet iron	127	0.076
Cardboard	277	0.043

the temperature of the tube and its air column to be stabilized, the temperature difference between the air at the top of the tube and that at the bottom of the tube was found to be a negligible fraction of 1° C. This seemed hardly sufficient to cause appreciable convection currents. A coat of petrolatum was applied to the inside of each of the glass tubes and to the cardboard tube in an effort to arrest the further fall of any grains that might be attracted to the sides of these tubes. The cardboard tube was tested both dry and with petrolatum coating. It will be noted that the petrolatum coated tube seemed to yield a rate of fall approximately 10 per cent slower than that yielded by the dry tube. An iron pipe was finally selected for extended experiment because it yielded slower rates of fall than any of the other chambers used and because, theoretically, it should, as set up, have eliminated many of the electrical perturbations.

APPARATUS AND TECHNIQUE

The original data shown in this paper (except in Table II) were secured by measuring the average time of fall and calculating the average rate of fall of various pollens in an iron water pipe, 48 in. long and of 51 mm. inner diameter (Fig. 1), placed vertically in an unventilated, unheated inner room. The iron pipe and its support were grounded by a heavy metal strip fastened to a service water pipe line. The tube was equipped at the top with a horizontal swinging gate which allowed rapid opening and closing without exerting either positive or negative pressure on the air column in the tube. The bottom of the tube was closed except for an opening 1 cm. square in the center of the closure. Even this opening was kept closed except during the actual changing of slides. The bottom of the tube cleared the slide table just sufficiently to allow glass slides to be passed under it without disturbing their oiled surface.

The pollen to be tested was blown from a dry atomizer into a glass beaker of approximately 500 c.c. capacity, which was coated on the inside with petrolatum. If the beaker were held at the optimum horizontal distance from the outlet of the atomizer (usually about 8 inches), a well-dispersed cloud of pollen could be caught in it. A portion of this suspended pollen cloud was then quickly delivered to the momentarily opened tube by passing the inverted beaker over the opening with a slow horizontal motion. Slides for catching the pollen grains

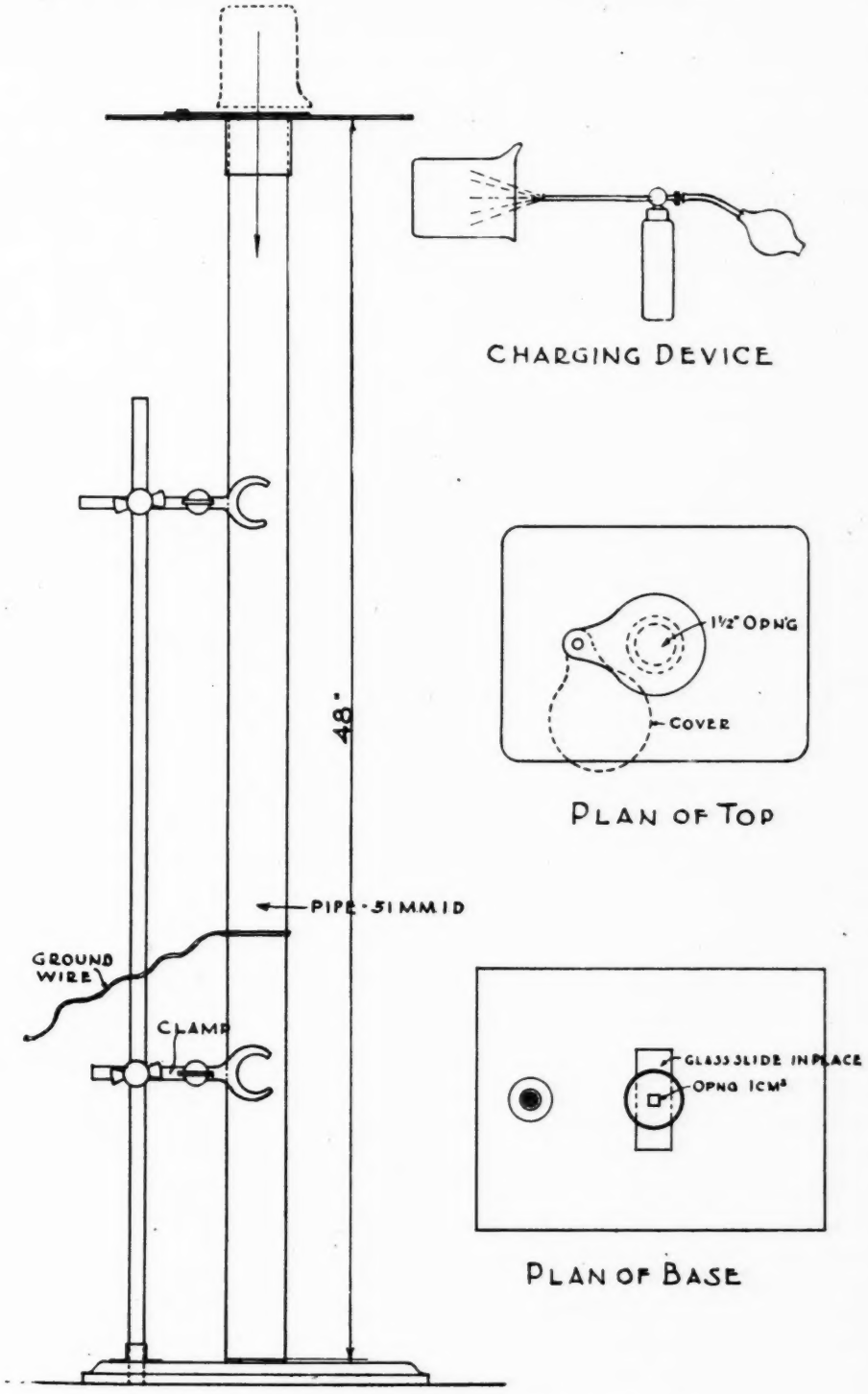

Fig. 1.—Apparatus for testing rate of fall of pollen.

at the bottom of the air column were placed under the center of the tube; changes were made every five seconds by pushing each exposed slide out with its successor.

TABLE III. RATE OF FALL OF COCKLEBUR POLLEN (LOT B) IN STILL AIR
(Five tests in iron tube 48 in. long, 51 mm. inner diameter)

SECONDS	NUMBER OF POLLENS CAUGHT DURING FIVE-SECOND PERIOD				
0	0	0	0	0	0
65	0	0	0	12	1
70	3	1	4	216	43
75	8	0	18	204	195
80	47	3	41	78	100
85	67	9	36	29	79
90	25	10	22	8	19
95	16	2	14	2	7
100	7	5	2	2	6
105	0	0	0	0	4
Average time of fall	87.7	91.3	87.0	76.6	81.3

Mean for first three tests 88.7 seconds
Mean for last two tests 78.9 seconds

Average rate of fall for first three tests 0.045 ft. per second
Average rate of fall for last two tests 0.051 ft. per second

The number used to designate the amount of pollen caught in each five-second period, as shown in the figures in Table III, is not the total number of pollen grains passing through the 1 sq. cm. opening at the bottom of the air column but is a figure obtained by counting the grains seen with the microscope in five consecutive trips all the way across the slide through the area of heaviest deposit (approximately 0.55 sq. cm. of the exposed surface). However, more than five trips were always counted, so that the figure used represents the maximum count for any five *adjacent* trips. In calculating the time of fall it was assumed for simplicity that all of the pollen grains appearing on a slide exposed, as for example, between seventy-five and eighty seconds after the charge was imparted, fell in an average time of 77.5 seconds.

BEHAVIOR OF FREE-FALLING POLLEN GRAINS

It must be emphasized that although the cloud of pollen grains is delivered to the top of the air column in considerably less than one second (estimate, one-fourth second), the individual grains do not all traverse the 4-foot column in the same length of time. Some of their variation in velocity is doubtless due to differences in the size of the pollen grains. In some species there is a considerable lack of uniformity in size; in other species there is very little. Another factor which might seem to be more important than the one mentioned is the static charge imparted to the individual granules in their violent expulsion from the atomizer. This charge must continue to operate in driving the particles farther and farther apart as they fall. But when the atomizer was dispensed with and the pollen was introduced by being dislodged from a card, no appreciable difference in velocity was obtained.

When the atomizing is improperly done, large clumps of pollen and many aggregates of two, three, or more cohering granules may reach the bottom of the air column before any of the single granules. Obviously, the larger the size of an aggregate, the more rapidly it falls. Thus when a charge is too heavy it doubtless creates air currents which tend to drag down some of the single granules faster than they would normally fall in still air. Dyakowska does not mention this point in her paper, but I have found it to be very important. It is also quite evident, from the figures in Table III, that when too much pollen is introduced, even though the grains are well dispersed, the rate of fall is greatly

TABLE IV. COMPARISON OF RATES OF FALL AS DETERMINED BY FOUR DIFFERENT INVESTIGATORS
(Data in Centimeters Per Second)

COMMON NAME	BOTANICAL NAME	DIAMETER IN MICRONS*	CALCULATED RATE†	EXPERIMENTAL RATE			
				BODMER	KNOLL	DYAKOWSKA	DURHAM
Scotch pine	*Pinus sylvestris*	40.0	–	3.7			
Scotch pine	*Pinus sylvestris*	52.0	–		2.5	3.69	2.49
Bull pine	*Pinus ponderosa*	60.0	–				3.49
Ash	*Fraxinus excelsior*	25.0	1.71	0.75			
Ash	*Fraxinus*	38.0	3.9			5.21	
Ash	*Fraxinus*	27.1	2.0				1.52
Poplar	*Populus*	25.4	1.54			3.39	
Poplar	*Populus virginiana*	30.0	2.14				1.52
Elm	*Ulmus montana*	30.0	2.71	1.95			
Elm	*Ulmus glabra*	26.9	2.20			3.24	
Elm	*Ulmus americana*	31.2	2.95				2.04
Hazelnut	*Corylus avellana*	30.0	2.96	1.95	2.5		
Hazelnut	*Corylus avellana*	24.2	1.89			2.9	
Hazelnut	*Corylus americana*	23.6	1.83				1.31
Walnut	*Juglans regia*	40.0	4.48	3.65			
Walnut	*Juglans nigra*	35.7	3.61				2.84
Oak	*Quercus robur*	27.7	2.41		2.9	3.96	
Oak	*Quercus imbricaria*	33.1	3.42				2.20
Oak	*Quercus macrocarpa*	32.3	3.30				1.83
Alder	*Alnus glutinosa*	30.0	2.59	1.95			
Alder	*Alnus viridis*	30.0	2.59		1.7		
Alder	*Alnus glutinosa*	26.0	1.98				1.46
Birch	*Betula verrucosa*	25.0	1.78	1.5			
Birch	*Betula verrucosa*	24.5	1.68			2.94	
Birch	*Betula pubescens*	27.5	2.13			2.94	
Birch	*Betula nigra*	24.6	1.70				1.68
Hemp	*Cannabis sativa*	30.0	2.22	2.55			
Hemp	*Cannabis sativa*	25.0	1.56				1.04
Orchard grass	*Dactylis glomerata*	34.0	3.17		3.1		2.78
Timothy	*Phleum pratense*	34.0	3.17				2.80
Rye	*Secale cereale*	60.0	10.88	7.4			
Rye	*Secale cereale*	49.5	7.25				4.30
Corn	*Zea mays*	90.0	24.52	26.0			18.00
Average deviation from calculated rate:				-21%	-10%	+61%	-26%

*My measurements made on grains expanded in Calberla's solution.
†Using Stokes' law and correcting for specific gravity with data shown in Table V.

increased. Whether this is an air current effect or an electrical effect is not clear.

Table IV shows a comparison of my results with those of Bodmer, Knoll, and Dyakowska, involving pollens mostly of the same genus but occasionally of the same species or only of the same family. In this particular table the velocity data are given in centimeters per second rather than feet per second because the original figures of the European workers are thus stated and because the larger whole numbers involved are more readily compared. It will be seen that in my air chamber the rate of fall of every one of these pollens was slower than the calculated rate and that the average difference was 26 per cent. Bodmer's results are, in general, about the same as mine, while for Knoll the average rate was faster than that obtained by Bodmer. Dyakowska's rates average 62 per cent faster than the calculated rates and more than twice as fast as mine. By way of explanation of this interesting situation, it is only necessary to note that Bodmer, as well as Knoll, used an air chamber of much smaller diameter than that used by Dyakowska. Moreover, Table II shows that when I used an air chamber with a diameter similar to the one used by Dyakowska I also more than doubled the rate of fall for ragweed pollen as compared with the rate obtained with the smaller chamber.

RESULTS OF EXPERIMENTS

Under the uniform conditions noted, rates of fall have been determined for pollens of 38 species. In Table V these rates are compared with the calculated rate obtained by using Stokes' formula, including the density (specific gravity) factor.[4] Of all the pollens tested only the ragweeds and Russian thistle fell faster than their respective calculated rates. The performance of the ragweeds is particularly surprising in view of past assumptions about the slowing effect of the spicules on these pollens. The pollens of the ragweeds (except *Iva xanthifolia*) and Russian thistle are examples of a type of pollen grain which remains approximately spherical in the dry as well as the moist state, whereas the pollens of the trees, the grasses, and such weeds as the wormwoods, hemp and western water hemp shrink considerably in drying. Whether the apparent differences in relative buoyancy as brought out in this study are due more to the irregular surfaces of the pollen grains or to my errors in measurement of size and weight is not certain. (All measurements of diameters are made on grains expanded in Calberla's solution). It is barely possible that my figures for the specific gravity of ragweed are too low, thus causing the calculated rates to also be lower than they should be. I am quite sure, however, that if the density determinations are in error at all the figures are too high rather than too low.

Finally, I am not absolutely certain that the air in my iron tube remains perfectly still either before or after the introduction of a charge of pollen. All of my velocity figures may be too high or they may be too low, but the important point is that when determined under uniform conditions they are remarkably consistent, within the different botanical groups, in their conformity to the principles of Stokes' law.

Indeed, a long step has been made toward the goal of volumetric interpolation of gravity slide figures when *relative* rates of fall have been established for pollen grains of various shapes, sizes, and surface characters. As a result of this study it is evident that, since pollens like bluegrass, Russian thistle, and oak fall twice as fast as those of common ragweed, a *true* gravity count of these

TABLE V. ORIGINAL DATA ON SPECIFIC GRAVITY AND RATES OF FALL

LOT SYMBOL	COMMON NAME	BOTANICAL NAME	DIAMETER IN MICRONS*	SPECIFIC GRAVITY†	RATE OF FALL IN FEET PER SECOND		EXPERIMENTAL RATE AS COMPARED WITH SHORT RAGWEED
					CALCULATED	EXPERIMENTAL	
AA	Giant ragweed	*Ambrosia trifida*	19.25	0.52	0.019	0.027	0.93
N	Burweed marsh elder	*Iva xanthifolia*	19.3	0.79	0.029	0.031	1.07
A	Short ragweed	*Ambrosia elatior*	20.0	0.55	0.022	0.029	1.00
CC	False ragweed	*Franseria acanthicarpa*	22.0	0.75	0.036	0.033	1.14
I	Marsh elder	*Iva ciliata*	23.0	0.58	0.031	0.039	1.34
P	Southern ragweed	*Ambrosia bidentata*	23.0	0.50	0.026	0.038	1.31
BB	Western ragweed	*Ambrosia psilostachya*	26.4	0.57	0.039	0.046	1.59
B	Cocklebur	*Xanthium commune*	27.0	0.45	0.032	0.045	1.55
G	Russian thistle	*Salsola pestifer*	23.6	0.90	0.050	0.061	2.10
S	Palmer's amaranth	*Amaranthus palmeri*	25.8	1.02	0.067	0.061	2.10
O	Western water hemp	*Acnida tamariscina*	27.5	1.01	0.076	0.048	1.66
HH	Mexican fireweed	*Kochia scoparia*	32.7	0.97	0.104	0.094	3.24
Q	Annual sage	*Artemisia annua*	20.4	1.02	0.042	0.033	1.14
J	Tall wormwood	*Artemisia caudata*	21.0	1.04	0.046	0.032	1.10
PP	Sagebrush	*Artemisia tridentata*	25.85	1.03	0.068	0.052‡	1.79
F	Nettle	*Urtica gracilis*	14.0	0.77	0.013	0.011‡	0.38
H	Red sorrel	*Rumex acetosella*	21.45	0.78	0.036	0.031	1.06
V	Hemp	*Cannabis sativa*	25.0	0.82	0.051	0.034	1.17
EE	English plantain	*Plantago lanceolata*	27.5	0.97	0.073	0.049	1.69
C	Bluegrass	*Poa pratensis*	28.0	0.90	0.070	0.048	1.66
NN	Bluegrass	*Poa pratensis*	30.0	0.90	0.080	0.057	1.97
FF	Bermuda grass	*Capriola dactylon*	28.5	1.01	0.082	0.061	2.10
Z	Orchard grass	*Dactylis glomerata*	34.0	0.91	0.105	0.091	3.14
D	Timothy	*Phleum pratense*	34.0	0.90	0.104	0.092	3.17
OO	Rye	*Secale cereale*	49.5§	0.98	0.238	0.141	4.86
E	Corn	*Zea mays*	90.0	1.00	0.804	0.600	20.7
JJ	Sycamore	*Platanus occidentalis*	22.22	0.92	0.045	0.034	1.18
GG	Mountain cedar	*Juniperus sabinoides*	22.8	1.08	0.056	0.038	1.31
X	Hazelnut	*Corylus americana*	23.6	1.09	0.060	0.043	1.48
T	Birch	*Betula nigra*	24.6	0.94	0.056	0.055	1.90
L	Alder	*Alnus glutinosa*	26.0	0.97	0.065	0.048	1.66
M	Ash	*Fraxinus americana*	27.1	0.90	0.066	0.050	1.72
U	Cottonwood	*Populus virginiana*	30.0	0.79	0.070	0.050	1.72
W	Elm	*Ulmus americana*	31.2	1.00	0.097	0.067	2.31
Y	Bur oak	*Quercus macrocarpa*	32.3	1.04	0.108	0.060	2.07
H	Shingle oak	*Quercus imbricaria*	33.1	1.04	0.112	0.072	2.48
K	Walnut	*Juglans nigra*	35.75	0.93	0.118	0.093	3.21
DD	Beech	*Fagus grandifolia*	44.0	0.94	0.181	0.116	4.00
R	Hickory	*Carya ovata*	45.0	0.79	0.159	0.074	2.55
LL	Scotch pine	*Pinus sylvestris*	52.0‖	0.45	–	0.082	2.82
KK	Bull pine	*Pinus ponderosa*	60.0‖	0.45	–	0.115	3.95

*All measurements made on grains expanded in Calberla's solution.
†As determined by experimental methods described in the first paper of this series.[9]
‡As calculated by performance of other similar granules.
§Mean of long and short diameters.
‖Measured exclusive of wings.

pollens should be discounted 50 per cent in order to have an approximately correct idea of the number of pollen grains in a given volume of air as compared to common ragweed. It follows that true gravity figures for timothy pollen, which falls more than three times as fast as ragweed pollen, should be discounted 70 per cent, and rye, which falls five times as fast, should be discounted 80 per cent, whereas gravity figures for hemp, annual sage, or sycamore would need to be discounted less than 20 per cent.

TABLE VI. EXCESS OR DEFICIENCY OF EXPERIMENTAL RATES OF FALL AS COMPARED WITH CALCULATED RATES

(Data from Table V)

Ragweeds	
Giant ragweed	+42%
False ragweed	- 8%
All ragweeds, average	+23%
Chenopods and amaranths	
Western water hemp	-37%
Russian thistle	+22%
All chenopod-amaranths, average	-25%
Wormwoods, average	-25%
Grasses	
Rye	-41%
Timothy	-11%
All grasses, average	-26%
Trees (not including pine)	
Hickory	-53%
Birch	-2%
All trees, average	-33%
All pollens tested, average	-24%

But since outdoor air is never still, gravity is not the only factor involved in the deposit of aero-allergens on "gravity" slides. So the ultimate usefulness of the data in this paper must depend on further studies on the actual outdoor performance of pollens and fungus spores as discussed in the second paper of this series.[10] Briefly, the method consists in standardizing the deposit on gravity slides exposed under controlled conditions against the actual number of pollen grains recovered from a given volume of air.

REFERENCES

1. Scheppegrell, W.: Hay-Fever and Hay-Fever Pollens, Arch. Int. Med. **19**: 959, 1917.
2. Cocke, E. C.: Calculating Pollen Concentration of the Air, J. ALLERGY **8**: 601, 1937.
3. Cocke, E. C.: A Method for Determining Pollen Concentration of the Air, J. ALLERGY **9**: 458, 1938.
4. Dahl, A. O., and Ellis, R. V.: The Pollen Concentration of the Atmosphere, Pub. Health Rep. **57**: 369, 1942.
5. Dyakowska, J.: Researches on the Rapidity of the Falling Down of Pollen of Some Trees, Cracow, Acad. Polon. Sciences; Bull. Internat. (B) (I), **155**: 1936-1937.
6. Pohl, F.: Die Pollenkorngewichte einiger windblütiger Pflanzen und ihre ökologische Bedeutung, Beih. Bot. Centralbl., Abt. A **57**: 1937.
7. Bodmer, H.: Über den Windpollen, Natur u. Technik, 3, 1922.
8. Knoll, F.: Über die Fernverbreitung des Blütenstaubes durch den Wind, Forsch. u. Fortschr., Jahrg. 23, 1932.
9. Durham, O. C.: The Volumetric Incidence of Atmospheric Allergens. I. Specific Gravity of Pollen Grains, J. ALLERGY **14**: 455, 1943.
10. Durham, O. C.: The Volumetric Incidence of Atmospheric Allergens. II. Simultaneous Measurements by Volumetric and Gravity Slide Methods. Results With Ragweed Pollen and Alternaria Spores, J. ALLERGY **15**: 226, 1944.

THE VOLUMETRIC INCIDENCE OF ATMOSPHERIC ALLERGENS

IV. A Proposed Standard Method of Gravity Sampling, Counting, and Volumetric Interpolation of Results

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SINCE the degree of contact of the sensitive person with air-borne allergens is strictly determined by the number of allergenic particles brought into his respiratory organs in a given volume of inhaled air during a very short period of exposure, it follows that the most logical measure of allergenic air contamination should be some convenient volumetric unit. This was first recognized by Blackley.[1] But so far no satisfactory volumetric sampling apparatus has been devised. It is true that several types of volumetric dust counters are altogether practicable for spot tests and short-run pollen sampling, but the usefulness of such instruments in allergy research has not been exploited, largely because we have had no basis for comparing the results yielded by them with the figures obtained from gravity slide tests. No reliable volumetric device has yet been found which will run unattended twenty-four hours a day, for months at a stretch, furnishing an unbroken series of seasonal air samples that can be easily counted. So the gravity method of sampling (adhesive coated slides held in a horizontal position) remains our only practicable source of seasonal aeroallergen data. I am convinced that we must make the best of it.

Efforts to interpret gravity slide figures in volumetric equivalents have from the start been hampered, first, by unwarranted assumptions as to the behavior of free-falling particles in outdoor air, second, by a completely erroneous table of conversion factors (based on Stokes' law) that stood unchallenged for nearly twenty years,[2, 3] and, third, by the lack of a standard exposure apparatus for gravity slides.

LOCATION OF SAMPLING STATION

Since the greatest need for atmospheric pollen research is in the urban areas where the majority of the hay fever sufferers reside, it should be recognized at the outset that the "absolute pollen frequency of the air"[4] differs widely at a given moment in various parts of any city and fluctuates greatly from hour to hour, as well as from day to day, in a given location. We must also recognize that buildings, trees, and other objects cause unavoidable air turbulence and unpredictable air currents that greatly influence the deposit of pollen on gravity slides. Therefore, since no ideal testing location can possibly be found or arranged, the only type of location that can be regarded as *standard* for obtaining a typical daily average measure of city-wide air contamination is the top of a tall building in the downtown section—a point farthest from possible local sources of air pollution. The roof chosen should be level and, if possible, free from obstructions. If not, the spot on it chosen for exposures should be as far from obstructions as possible. When gravity tests are made in residence parts

*From the Biological Laboratories of Abbott Laboratories.

of the city the flat roof of an apartment building would be most likely to yield data comparable to those of a downtown location. Porches and window ledges are not recommended, but special and unusual locations may, of course, be suitable for the study of special local exposure problems. Certainly in reporting results of any atmospheric survey the sampling location should be stated and described or pictured in detail.

A STANDARD GRAVITY SAMPLING DEVICE

The simplest possible apparatus for exposing gravity slides is a flat, unobstructed, horizontal plane on which a prepared slide may be laid face up. The major objections to this method are that it affords no protection from rain, that even a smooth horizontal surface is known to cause a ripple effect on air currents flowing over it, and that dust and other particles falling on the dry surface of any area larger than the slide may be subsequently swept directly onto the adhesive surface of the slide. In practice, such an exposure results in a heavier catch than an exposure at the same spot which allows air to flow under as well as over the slide.

The need of protection for the slide from the fall of soot and large airborne particles and from the direct wash of rain has led most workers to adopt some sort of cover for the slide. A popular form of shelter[5] consists of a dome-shaped metal tunnel having openings cut in each side. The slide is usually placed in the center of this shelter flat on the floor. Such a device might recover comparable proportions of the pollen content of the air at each exposure if mounted on a wind vane so that the open end of the tunnel would always face the wind, but obviously without such a mounting the turbulence and the consequent effect on pollen impingement must differ greatly with any change in wind direction.

In my nation-wide studies at the U. S. Weather Bureau stations[6] the slides have usually been held in a wooden clip placed about 1 foot beneath the Weather Bureau's instrument shelter which is some 4 feet square. These instrument shelters are usually located on top of tall business buildings. The deposits of ragweed pollen on slides exposed by any of the above methods (other exposure factors being similar) average considerably heavier than the deposits on slides exposed by methods to be described.

In two series of experiments[7] carried out on a large four-story building in North Chicago (1942, 1943), I exposed slides in a horizontal position on top of a 3-foot iron rod, without a shelter of any sort. This very simple device offered the least possible interference to passing wind currents, but in spite of this the day by day deposit was far from uniform in proportion to the daily average ragweed pollen content of the air as measured by parallel tests with the Hawes volumetric impinger* or the Keitt volumetric filter,* or both run simultaneously.

*The Hawes apparatus pulls approximately 0.1 cu. ft. of air per minute through a slit 10 mm. long and 0.2 mm. wide, impinging all particles on an adhesive slide held 2 mm. away from the slit. The slide is moved very slowly by clock work so that the deposit is left in a convenient swath. The Keitt apparatus pulls approximately 1 cu. ft. of air per minute through a nitrocellulose filter. The plug of nitrocellulose is dissolved and the pollen content is plated for counting.

Most of the gravity slides caught twice as much pollen per square centimeter as could possibly be accounted for by Stokes' law, but on some days the excess was as much as six times the calculated amount.

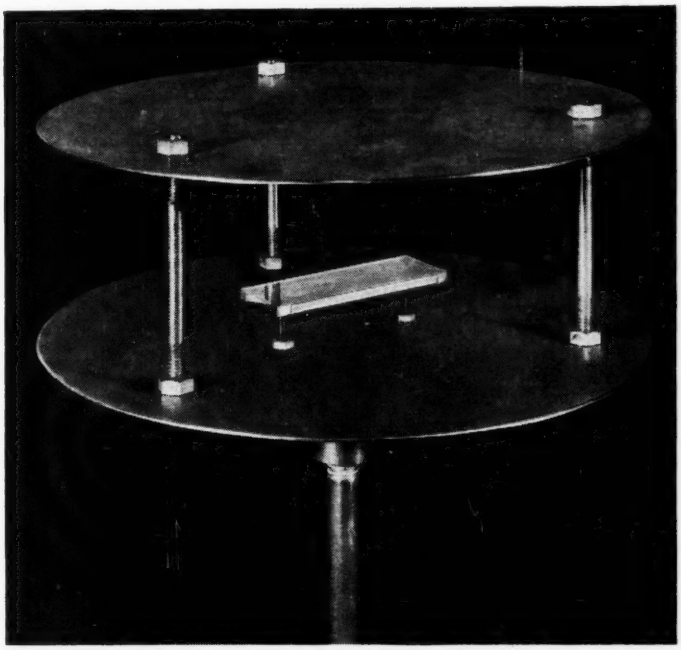

Fig. 1.—Standard air-sampling device. The apparatus consists essentially of two parallel planes of polished stainless steel, 9 inches in diameter, with the slide holder raised 1 inch above the lower plane. It is supported by a 30-inch metal rod on a tripod laboratory stand. Screw holes are provided in the base so that it may be fastened securely to any wooden floor.

The device pictured in Fig. 1 makes use of two parallel planes of polished stainless steel held in position by three narrow struts. The purpose of these planes, aside from the rain protection afforded by the upper one, is to cause an even horizontal flow of air between them regardless of the direction or velocity of the wind. As used in the 1944 experiments, the oiled surface of the slide was held *flush* with the surface of the lower plane which was itself oiled in order to fix all pollen and other particles falling on it. In the form shown here and used for making comparative exposures during 1945, the slide holder is elevated 1 inch above the lower plane, thus allowing the air stream to flow underneath as well as over the slide. This has resulted in a smaller deposit of pollens and spores (as compared with our parallel volumetric determinations), thus more nearly approaching the ideal calculated gravity deposit.

The need of a standardized method of exposure is strongly emphasized by the tabulated results (Table 1) of exposures with this improved, proposed standard device as compared with parallel exposures in shelters of varying design as noted. These shelters were, in each locality, the ones which have been used for a number of years by the individual local collaborators.

TABLE I. GRAVITY TEST COMPARISONS: RAGWEED SEASON, 1945

PLACE	DESCRIPTION OF OLD SHELTER	NUMBER OF DAYS	TOTAL CATCH		RATIO (NEW/OLD)
			NEW DEVICE	OLD SHELTER	
New York, N. Y., U. S. Weather Bureau, Central Park, ground level	6 inch vertical space between large covers, open at west and east ends	22	444	624	1.41
Brooklyn, N. Y., Jewish Hospital; roof; 5 stories	Metal tunnel; slide flat on floor	22	274	1,488	5.43
Philadelphia, Pa., Elverson Medical Building, 15th floor	Metal tunnel; slide elevated with air clearance under slide	48	2,817	3,798	1.35
Pittsburgh, Pa., Montefiore Hospital; roof; 4 stories	Wood tunnel, gable roof; slide elevated 1 inch on block	46	395	510	1.28
Pittsburgh, Pa., suburban residence, Penn Township; ground level	Same as above	50	2,574	2,371	0.92
Cleveland, O., Carnegie Medical Building; roof; 9 stories	Metal tunnel	43	657	804	1.63
Toledo, O., Medical Building; roof; 9 stories	Wood gable roof on two posts	50	2,998	6,034	2.01
Madison, Wis., Wisconsin General Hospital; roof; 6 stories	Wood roof supported by four corner posts	41	2,286	5,909	2.58
Milwaukee, Wis., U. S. Weather Bureau; P. O. Building; roof; 7 stories	Under U. S. Weather Bureau standard instrument shelter	4	378	1,573	4.16
North Chicago, Ill., Research laboratory; roof; 3½ stories	Shelter roof 24 in. square; 5 in. clearance	13	393	1,473	3.75
Chicago, Ill., Old P. O. Building; roof; 9 stories	Under U. S. Weather Bureau standard instrument shelter	30	645	1,704	2.61
Nashville, Tenn., Doctors Building	Parallel wood planes 18 in. by 21 in.; 5 in. clearance; 4 corner posts	44	1,914	2,424	1.27
Dallas, Tex., Medical Arts Building; 17 stories		70	9,512	11,356	1.19

CALIBRATION OF SAMPLING DEVICE

Finally, it was necessary to determine the average recovery of a given kind of pollen with this new proposed standard device as compared with the amount of that particular pollen in a cubic yard of air. A series of 17 tests (approximately 136 hours) were carried out using the gravity sampling device in parallel with the Hawes impinger during the ragweed season of 1945 (Table II). Part of the tests were made on the roof of a 3-story research laboratory building in North Chicago and part on the 7-story annex of the post-office building in Milwaukee. While air samples of ragweed, taken with the device, contained on the average nearly three times as much pollen as would be predicted by Stokes' law (using my experimental rate of fall for short ragweed for purposes of calculation), the daily figures were more consistent in their relation to the daily volumetric ragweed pollen determinations than those obtained with uncovered slides and much more consistent than those from gravity slides exposed by the old Weather Bureau method. The volumetric control tests made in parallel with each gravity test showed an average of 3.6 times as many ragweed pollen grains per cubic yard of air as were deposited on 1 sq. cm. of the gravity slides

TABLE II. EXPERIMENTAL RATING OF STANDARD SAMPLING DEVICE

PLACE	DATE 1945	GRAVITY: POLLENS PER SQ. CM. IN 24 HR.	VOLUMETRIC: POLLENS PER CU. YD. OF AIR, AVERAGE	RATIO GRAVITY/ VOLUME
North Chicago	August 20	34	110	3.2
North Chicago	August 24	100	254	2.5
North Chicago	August 26	9	10	1.1
North Chicago	August 27	169	273	1.6
North Chicago	August 28	111	681	6.1
Milwaukee	August 30	47	180	3.8
Milwaukee	August 31	222	821	3.7
Milwaukee	September 2	57	130	2.3
Milwaukee	September 3	52	115	2.2
North Chicago	September 5	66	407	6.2
North Chicago	September 6	30	202	6.7
North Chicago	September 7	113	159	1.4
North Chicago	September 9	68	478	7.0
North Chicago	September 10	45	201	4.4
North Chicago	September 11	45	183	4.1
North Chicago	September 12	16	38	2.4
North Chicago	September 19	10	55	5.5
Totals		1,194	4,297	
Ratio of totals				3.6

exposed for twenty-four hours. (For shorter exposure periods than twenty-four hours a larger equivalent area was counted).

STANDARD CONVERSION FACTORS

I suggest that the above factor—3.6—be regarded for present purposes as a standard conversion factor for ragweed air sampling *with this instrument* in areas where short ragweed is predominant. Thus an approximation of the average number of ragweed pollen grains per cubic yard of air for a twenty-four-hour period may be obtained either by counting an area of 1 sq. cm. on a twenty-four-hour slide and multiplying by 3.6 or by counting an area of 3.6 sq. centimeters. Since this latter area happens to be just twice the area that has been so widely used (1.8 sq. cm.), this part of the counting and interpolation will offer little difficulty.

If this ragweed factor proves to be acceptable it may be used as a pivot for establishing conversion factors for all other types of pollen found on slides exposed in the described standard apparatus. This can be done, as will be shown shortly, by means of the figures which I have already determined experimentally for the relative rates of fall of pollen grains of some 40 other species of hay fever plants.

At this point an important question will naturally arise concerning the fact that a considerable part of the deposit on any slide is evidently caused by impingement rather than by gravity. How can we then apply rate of fall data as though all of the deposit were the result of the action of gravity? The answer is that centrifugal force acts in much the same way as gravity in sorting particles of different weights. The heavier particles in the air are impinged in greater proportion than the lighter particles, the latter tending to remain in the air and be carried around the edge of the slide which intercepts the air current.

TABLE III. CONVERSION FACTORS FOR TYPICAL POLLENS

COMMON NAME	BOTANICAL NAME	DIAMETER IN MICRONS	EXPERIMENTAL RATE OF FALL AS COMPARED WITH SHORT RAGWEED	A FACTOR FOR 1 SQ.CM.	B FACTOR FOR 3.6 SQ.CM.
Giant ragweed	*Ambrosia trifida*	19.25	0.93	3.87	1.08
Burweed marsh elder	*Iva xanthifolia*	19.3	1.07	3.36	0.93
Short ragweed	*Ambrosia elatior*	20.0	1.00	3.60	1.00
False ragweed	*Franseria acanthicarpa*	22.0	1.14	3.16	0.88
Marsh elder	*Iva ciliata*	23.0	1.34	2.69	0.75
Southern ragweed	*Ambroisia bidentata*	23.0	1.31	2.75	0.76
Western ragweed	*Ambrosia psilostachya*	26.4	1.59	2.26	0.63
Cocklebur	*Xanthium commune*	27.0	1.55	2.32	0.65
Russian thistle	*Salsola pestifer*	23.6	2.10	1.71	0.48
Palmer's amaranth	*Amaranthus palmeri*	25.8	2.10	1.71	0.48
Western water hemp	*Acnida tamariscina*	27.5	1.66	2.17	0.60
Mexican fireweed	*Kochia scoparia*	32.7	3.24	1.11	0.31
Annual sage	*Artemisia annua*	20.4	1.14	3.16	0.88
Tall wormwood	*Artemisia caudata*	21.0	1.10	3.27	0.91
Sagebrush	*Artemisia tridentata*	25.85	1.79	2.01	0.56
Nettle	*Urtica gracilis*	14.0	0.38	9.47	2.63
Red sorrel	*Rumex acetosella*	21.45	1.06	3.40	0.94
Hemp	*Cannabis sativa*	25.0	1.17	3.08	0.85
English plantain	*Plantago lanceolata*	27.5	1.69	2.13	0.59
Bluegrass	*Poa pratensis*	28.0	1.66	2.17	0.60
Bluegrass	*Poa pratensis*	30.0	1.97	1.83	0.51
Bermuda grass	*Capriola dactylon*	28.5	2.10	1.71	0.48
Orchard grass	*Dactylis glomerata*	34.0	3.14	1.15	0.32
Timothy	*Phleum pratense*	34.0	3.17	1.14	0.32
Rye	*Secale cereale*	49.5	4.86	0.74	0.21
Corn	*Zea mays*	90.0	20.7	0.17	0.05
Sycamore	*Platanus occidentalis*	22.22	1.18	3.05	0.85
Mountain cedar	*Juniperus sabinoides*	22.8	1.31	2.75	0.76
Hazelnut	*Corylus americana*	23.6	1.48	2.43	0.68
Birch	*Betula nigra*	24.6	1.90	1.89	0.53
Alder	*Alnus glutinosa*	26.0	1.66	2.17	0.60
Ash	*Fraxinus americana*	27.1	1.72	2.09	0.58
Cottonwood	*Populus virginiana*	30.0	1.72	2.09	0.58
Elm	*Ulmus americana*	31.2	2.31	1.56	0.43
Bur oak	*Quercus macrocarpa*	32.3	2.07	1.74	0.48
Shingle oak	*Quercus imbricaria*	33.1	2.48	1.45	0.40
Walnut	*Juglans nigra*	35.75	3.21	1.12	0.31
Beech	*Fagus grandifolia*	44.0	4.00	0.90	0.25
Hickory	*Carya ovata*	45.0	2.55	1.41	0.39
Scotch pine	*Pinus sylvestris*	52.0	2.82	1.28	0.35
Bull pine	*Pinus ponderosa*	60.0	3.95	0.91	0.25

Formula for deriving factors in columns *A* and *B*:

$$\text{Factor A} = \frac{3.6}{\text{comparative rate of fall}} \qquad \text{Factor B} = \frac{A}{3.6}$$

This I have verified a number of times by whirling an oil-coated slide through the air, oiled face forward, at a rate of approximately 50 miles per hour. Such a slide picks up a much smaller proportion of the lighter particles in the air, such as *Alternaria,* than of the heavier ragweed pollen grains as compared with the number of each in the air as shown by simultaneous volumetric sampling. Moreover, in the course of my four seasons' experience with gravity sampling controlled with volumetric tests, I have found that the more buoyant particles such as nettle pollen grains and *Alternaria* spores actually produce lighter "gravity"

deposits than ragweed, while heavier pollen grains such as Mexican fireweed, western water hemp, and hemp produce heavier deposits in about the expected proportion.

As a result of these findings I feel justified in deriving standard conversion factors (as shown in Table III) from figures for comparative rates of fall as originally published in the third paper of this series.[8]

It must be noted that these factors apply only to gravity slide data from exposures in the apparatus described. Standardization of any other gravity sampling device which in the future may seem more acceptable than this one will require at least one season of daily volumetric control tests, preferably during a season of ample ragweed pollen incidence, and the development of a whole new set of conversion factors. In spite of variations in pollen grain size and specific gravity which necessarily affect the accuracy of the conversion factors here presented, it is quite likely that errors from these sources are much smaller than the inherent errors in any gravity sampling method. Extreme accuracy is an impossible goal in this field of research.

DISCUSSION

Factors are given for eight species of ragweed, six of which are of more or less restricted distribution. The amount of giant ragweed pollen in the air in most areas will hardly justify the use of a higher factor during the early part of the ragweed season. If in some areas the average size of air-borne ragweed pollen grains throughout the whole season or during the greater part of the season proves to be appreciably more or less than 20 microns, an adjusted factor should be used. The only other possible call for adjustment of the ragweed factor would be in the case of an experimenter finding the actual ratio of ragweed pollen per cubic yard of air to the number per square centimeter of slide at his place of sampling to be more or less than 3.6. Such a local factor could be established only by a long series of parallel volumetric and gravity tests.

The above suggestions apply to the use of all other factors for the typical pollens listed in Table III. If, for example, the poplar pollen grains found on the slides in a particular locality average smaller or larger than the 30-micron cottonwood pollen which I have tested, a different local conversion factor will need to be calculated. This may be derived as follows, assuming that local poplar species measures 32 microns in polar diameter (expanded in Calberla's solution or other aqueous medium).

$$\frac{32^2}{30^2} = \frac{2.09}{x}, \text{ solving}$$

$$x = \frac{30^2 \times 2.09}{32^2} = 1.84$$

Obviously no common factor can be used for grass pollens since the size of grass pollen granules varies considerably with the prevailing grass pollen in the air. The factor for redtop (diameter, 26 microns) will likely be about 2.8 and Canada bluegrass (diameter, 30 microns) about 1.97—as for bluegrass of that same diameter.

The set of factors in column *A* of Table III are to be used when the unit slide area counted is 1 sq. cm., but in case it is deemed more convenient to count a slide area of 3.6 sq. cm., by which method ragweed figures will not need to be converted, the factors for other pollens will be found in column *B*.

Factors for those types of fungus spores which may be identified on gravity slides are not yet available except for *Alternaria*. From extensive data on volumetric incidence and relative gravity deposit of ragweed pollen and *Alternaria* spores given in the second paper of this series, we seem justified in using *A* and *B* factors for *Alternaria* which are 4.14 times those of ragweed—factor *A*, 14.90; factor *B*, 4.14.

SUMMARY

This paper stresses the need of a standardized method of sampling, counting, and volumetric conversion of data for air-borne allergens. As a result of five seasons of experimentation with various gravity sampling devices controlled by parallel volumetric tests, the following proposals are submitted:

1. The basic index of atmospheric contamination in a given community should depend on aerobiologic data secured from air samples taken on the unobstructed top of a tall downtown building.

2. A practicable gravity sampling device (slide shelter) is pictured and described, and suggested as a tentative standard device. It has been used in a number of places during the past season and has been carefully rated as to the average proportion of ragweed pollen which it recovers from a cubic yard of air.

3. A method of volumetric conversion of pollen and fungus spore counts is submitted with definite factors for about 40 pollens and one fungus spore. Two sets of conversion factors are listed so that counting may be done on the basis of 1 sq. cm. of slide area or on 3.6 sq. centimeters.

The data for Table I were secured through the kind cooperation of the following allergists: J. Harvey Black, Dallas, Texas; George I. Blumstein, Philadelphia, Pa.; Leo H. Criep, Pittsburgh, Pa.; Milton S. Dunn, Pittsburgh, Pa.; Karl D. Figley, Toledo, Ohio; Harold J. Friedman, Cleveland, Ohio; William A. Mowry, Madison, Wis.; Edna S. Pennington, Nashville, Tenn.; and Matthew A. Walzer, Brooklyn, N. Y.

REFERENCES

1. Blackley, C. H.: Experimental Researches on the Cause and Nature of Catarrhus Aestivus (Hay Fever, or Hay Asthma), London, 1873, Baillière, Tindall & Cox.
2. Zifferblatt, A. H., and Seelaus, H. K.: A Study of Air Contaminants in the Interest of Public Health, Pennsylvania M. J. **39**: 67, 1935.
3. Cocke, E. C.: Calculating Pollen Concentration of the Air, J. ALLERGY **8**: 601, 1937.
4. Erdtman, G.: An Introduction to Pollen Analysis, Waltham, Mass., 1943, Chronica Botanica Company, p. 182.
5. Tuft, L.: Clinical Allergy, Philadelphia, 1938, W. B. Saunders Company, p. 596.
6. Durham, O. C.: The Pollen Content of the Air in North America, J. ALLERGY **6**: 128, 1935.
7. Durham, O. C.: The Volumetric Incidence of Atmospheric Allergens. II. Simultaneous Measurements by Volumetric and Gravity Slide Methods. Results With Ragweed Pollen and Alternaria Spores, J. ALLERGY **15**: 226, 1944.
8. Durham, O. C.: The Volumetric Incidence of Atmospheric Allergens. III. Rate of Fall of Pollen Grains in Still Air, J. ALLERGY **17**: 70, 1946.

SURVEY OF BRONCHIAL ASTHMA IN SOLDIERS: BRONCHOSCOPIC FINDINGS AND INCIDENCE OF RESPIRATORY INFECTION*

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INTRODUCTION

BRONCHIAL asthma has been a relatively common cause of medical disability in soldiers in World War II. Persons with disabling asthma have not been admitted into the Army in significant numbers. Many men, after entry into the service, have either developed asthma for the first time or suffered aggravation of pre-existing mild forms of the disease.

In addition to influences identified with civil life, bronchial asthma in soldiers is affected by many complex factors incident to the service. These include: unfavorable and unusual climates, frequent exposure to conditions favoring respiratory infections, psychic traumas of all types, combat fatigue, exposure to irritating dusts and gases, recurring febrile disease such as malaria, et cetera. Investigation of some of these aspects has already been reported (Leopold,[1] Hampton and Rand,[2] Blank,[3] and Alford[4]). This report is based upon a survey of 250 cases of perennial bronchial asthma in soldiers admitted to an Army general hospital. It is concerned primarily with two phases of the problem: (1) bronchoscopic findings, and (2) respiratory tract infection. These cases were selected consecutively from a group of patients with asthma in whom routine diagnostic study was augmented by bronchoscopic examination.

PROCEDURE

For each patient in this series, the completed diagnostic survey included the following procedures:

1. General medical check-up.

2. Allergy investigation. This consisted of an interview and examination by the consultant in allergy, intracutaneous tests with common inhalants, foods, molds, and pollens, and whatever other special allergy studies were indicated.

3. Nose and throat examination by the consultant otolaryngologist. A standard method was used for examining the nose and throat. The anterior nasal chamber was inspected in the usual manner—1 per cent ephedrine spray was used for shrinkage, and suction was employed as needed to demonstrate abnormal secretions. The nasopharynx was next observed with a mirror and, where indicated, with a Holmes nasopharyngoscope. Telltale evidence of infection was often found only in this region. In the oropharynx the tonsils were noted in addition to the lateral and posterior pharyngeal walls. Inspection of the lateral walls of the pharynx is often informative, for it may reveal red and

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edematous bands which represent a lymphangitis provoked by nasal and sinus infection. Transillumination and x-ray examination of the paranasal sinuses were performed in all cases. In this report, sinus diseases have been classified as either suppurative or nonsuppurative. The finding of mucopus was considered reliable evidence of bacterial infection, and the term "suppurative" was applied. "Nonsuppurative" was used to classify the remaining types of sinus disease, in which this criterion of infection was not observed. This group may include residual states of a suppurative infection when the bacterial invaders have been suppressed and only a relatively clear discharge remains.

4. Bronchoscopy. The use of bronchoscopy as a diagnostic aid in asthma was first advocated by Jackson[5] and later by Clerf,[6] who emphasized its importance in excluding other causes of bronchial obstruction simulating bronchial asthma. Andrews[7] stressed its added value in diagnosing the types of tracheobronchial change in bronchial asthma. In a discussion of Andrews' article, Unger contended that diagnostic bronchoscopy is indicated only in cases of asthma without an allergic background. The same point of view was affirmed by Tuft[8] and Feinberg.[9] Urbach and Gottlieb[10] urged the use of this procedure to determine the presence of complicating secondary bronchial infection.

In this series of cases, bronchoscopy was utilized for a twofold purpose: (1) to assist in excluding other conditions that simulate asthma, and (2) to demonstrate infection in the bronchi. Its use was governed not particularly by any type of bronchial asthma but rather by the need for more specific information in certain cases. One of the more urgent concerns in the management of soldiers with asthma is that of establishing a prognosis. Although any attempt at predicting the course of any individual case of asthma is admittedly precarious, the exigencies of the moment demanded that such an estimate be made so that proper therapy and disposition could be undertaken without delay. It was noted that on many occasions information supplied by bronchoscopy was of considerable value in deciding disposition. When chronic bronchial infection was revealed bronchoscopically, the asthma usually could not be satisfactorily controlled, regardless of how favorable the case appeared otherwise. Consequently, the occurrence of this complication was regarded as indicative of an unfavorable prognosis, and the asthma was evaluated accordingly. The value of bronchoscopy in this respect stimulated its use with increasing frequency.

The technique of bronchoscopy employed was a rather simple one. Nembutal was given the night preceding and one hour before examination. Dilaudid and scopolamine were administered one-half hour before the procedure. Pontocaine hydrochloride (2 per cent) was then applied topically to the oropharynx and pyriform sinuses. After the instrument was introduced, a Clerf atomizer was used to spray additional local anesthesia into the trachea and bronchi. The following features were carefully noted: (1) color of the membranes after they had been cleared of all discharge; (2) the nature and character of the bronchial secretions (these are often best judged when secured in a Tucker specimen taker and viewed in daylight, for material that appears purulent in the bronchi may be glary mucoid when seen outside, and vice versa); (3) changes in the thick-

ness of the membranes, as evidenced by loss of bronchial ring markings, and/or loss of sharpness of the septa of the secondary and tertiary bifurcations (favorite landmarks for estimating thickness are the mouth of the middle lobe and the mouth of the right and left dorsal branches of the lower lobe bronchi); and (4) the respiratory movements, especially the constriction concomitant with expiration. These are judged fairly only during quiet deep respirations when no pertussic impulse is present. In normal bronchi, the respiratory movements are so slight that they are barely perceptible.

RESULTS AND COMMENTS

General Findings.—Of the 250 soldiers comprising this series, 206 or 81.4 per cent had been on active duty overseas: European theater, 108; Southwest Pacific, 91; China-India-Burma, 7. Of this evacuated group, 71 developed their asthma for the first time while overseas, 48 in the Southwest Pacific, 21 in the European area, and 2 in the China-India-Burma area, indicating that the Southwest Pacific theater may be more conducive to the initiation of the disease. One hundred thirty-five of the overseas group gave a history of asthma prior to their transfer overseas. Of these, 117 (86.7 per cent) noted disabling aggravation of the condition after a variable period there. Our patients were predominantly young individuals—84 per cent were under 35 years of age and 30 per cent were under 25. The duration of the bronchial asthma varied as follows: less than one year's duration, 18.4 per cent; one to five years, 24.8 per cent; five to ten years, 15.2 per cent; over ten years, 41.6 per cent. The asthma was classified as severe if epinephrine injections were required to control symptoms, moderate if symptoms were marked enough to be disabling but not to require parenteral therapy, and mild if symptoms were not incapacitating. In this respect, 48.4 per cent of the cases were classified as severe, 48.8 per cent as moderate, and 2.8 per cent as mild. With but few exceptions all of the patients exhibited evidence of varying clinical activity during the period of our observation. Some had constant respiratory distress, while others had paroxysms of asthma with intervals of freedom varying from several days to several weeks. The skin reactions were entirely negative in 71 cases (28.4 per cent) and only questionably positive in 51 (20.4 per cent). In the remaining 128 patients (51.2 per cent), well-defined positive intracutaneous reactions to one or more allergens were noted. After all initial investigations had been completed and following a period of observation, an attempt was made to evaluate specific etiology in each case. Determination of specific causative factors with any certainty, within the relatively short period of observation, was not possible in the majority of cases. Our general impression was that extrinsic allergens were of definite etiological significance in about 20 per cent of the cases. About 40 per cent seemed to be primarily of intrinsic origin, and, in the remaining 40 per cent, no clear-cut estimate of etiology could be made.

Nose and Throat Findings.—The results of the rhinological examinations, summarized and classified with reference to sinus disease, are presented in Table I.

TABLE I. CLASSIFICATION OF RHINOLOGIC FINDINGS

DIAGNOSIS	NUMBER OF CASES	PER CENT
Chronic suppurative sinusitis	125	50.0
Chronic nonsuppurative sinusitis	16	6.4
No sinus disease	109	43.6
Total	250	100.0

Of the patients with chronic suppurative sinusitis, 32 per cent were classified as mild, 52 per cent as moderate, and 16 per cent as severe. Roentgenologic abnormalities were not infrequently noted in the group without sinus disease and were regarded as incidental allergic thickening of mucosa.

Bronchoscopic Findings.—Bronchoscopic findings in bronchial asthma have been described by a number of observers. It would seem that, in general, this procedure has been reserved for selected cases, commonly referred to as atypical, and the reported findings appear somewhat limited in scope. Clerf related two noteworthy findings, namely: (1) collapse of the tracheobronchial tree during coughing or forced expiration, and (2) the presence of abnormal secretions, described as thick mucoid and mucopurulent. A more comprehensive report was presented by Andrews, who stated that the most characteristic bronchoscopic finding in bronchial asthma was bronchitis. He describes the bronchoscopic appearance between acute attacks as divided into four general types: (1) minimal tracheobronchitis (mucosa is slightly reddened and secretions are small in amount); (2) chronic catarrhal tracheobronchitis (mucosa is dark red, sometimes cyanotic and velvety in appearance, and there are small amounts of nonpurulent secretion); (3) suppurative tracheobronchitis (mucosa is red and thickened and secretions are purulent); and (4) type not classified, in which the secretions are tenacious, thick, and adherent and difficult to remove. Andrews stated further that the bronchitis in the uncomplicated paroxysmal type of asthma is minimal, but that, as the condition becomes worse, or its duration prolonged, a chronic bronchitis develops. Urbach characterized the bronchial mucosa in the symptom-free interval as having a fairly normal or inflamed and velvety appearance if tracheobronchitis is present. During an attack, the lining mucosa is described as swollen, edematous, and purplish, and the bronchi are filled with a thick viscid secretion.

Bronchoscopy was completed in each case in this series of 250 patients, and the observations were recorded. Normal bronchial findings were noted in 26 cases. Bronchoscopic abnormalities of varied character were observed in the remainder. In only four patients did the bronchi present the so-called typical allergic appearance; that is, the mucosa was pale and edematous, and the secretions were watery and abundant. These changes were regarded as indicative of simple allergic activity in the bronchi and will not be discussed further. Our main concern was with the bronchoscopic abnormalities exhibited in the remaining 220 cases (88 per cent). Some degree of redness of the bronchial mucosa was noted in every patient in this group. This was accompanied by either increased thickness of the mucosa or alteration in the bronchial secretions or both. In the large majority of patients all three of these basic abnormalities were present.

The color of the mucous membranes varied from a mild redness to an intense fiery red; no purplish or cyanotic discolorations were observed. Mucosal thickening varied from a slight swelling to a mucosa so thick that it was thrown into folds. That this thickening was not merely transient edema was demonstrated by its failure to subside following application of epinephrine (1:1,000) by sponge or spray. The bronchial secretions were either normal in amount or increased and, in character, either uniformly mucoid or mucopurulent.

Early in the course of this study, it became essential to interpret and differentiate these bronchoscopic findings with respect to bronchial pathology. Adequate criteria for this purpose could not be obtained from previously published reports, and we were compelled to formulate our own. The changes in color and thickness of the mucosa and the alterations in bronchial secretion were regarded as indications of active inflammatory disease of the bronchi (bronchitis). On the basis of the character of the bronchial secretions, the bronchitis was differentiated as either suppurative or nonsuppurative. If the secretion appeared grossly purulent, the bronchitis was classified as infectious or suppurative. When the bronchial discharge was observed to be mucoid, the bronchitis was termed nonsuppurative. Cytologic and bacterial investigations of the bronchial secretions were important additional aids in making a differentiation between these two types of bronchial pathology. Although such studies were performed in many cases, they were not done in all, on account of circumstances beyond our control. Hence the results of laboratory examinations could not be utilized as diagnostic criteria in a strict sense. The element of chronicity was difficult to demonstrate on the basis of bronchoscopic findings alone and had to be judged by various features of the cases:

1. The clinical course of each case in this group was characteristic of a chronic disease in that the symptoms and findings were more or less unchanged over a long period of time. Nor were there any findings to suggest acuteness of the bronchial process at the time of bronchoscopy, such as sudden change in symptomatology, fever, leucocytosis, or increased sedimentation rate.

2. Bronchoscopy was repeated in a few cases in this group after intervening intervals of three to four weeks. No essential changes in the bronchoscopic findings were noted thereby.

3. Biopsied sections of the mucosa obtained at bronchoscopy were examined in six cases selected at random in this group. In all of these, chronic inflammatory changes (not purely allergic) were reported by the pathologist. The submucosa showed chronic inflammatory infiltrate composed of increased lymphocytes, plasma cells, and eosinophiles.

4. The bronchoscopic appearance was of some importance. In acute bronchitis, the mucosa appears fiery red and smooth. In the chronic cases it had a granular appearance, even though its color was fiery red at times.

Since all 220 cases were similar in one or more of the respects given, they were considered to have bronchitis in a chronic form. A summary of the bronchoscopic findings of the entire series is presented in Table II.

TABLE II. BRONCHOSCOPIC FINDINGS CLASSIFIED

TYPE OF BRONCHIAL PATHOLOGY	NUMBER OF CASES	PER CENT
No abnormality	26	10.4
Allergic bronchitis	4	1.6
Chronic suppurative bronchitis	123	49.2
Chronic nonsuppurative bronchitis	97	38.8
Total	250	100.0

The cases of chronic suppurative bronchitis were classified as mild in 32 per cent, moderate in 56 per cent, and severe in 12 per cent. In these patients, no significant correlation of the bronchitis to age, duration, or type of asthma could be demonstrated. In only a few of the patients with chronic nonsuppurative bronchitis were the extremely tenacious and viscid type of secretions found. The relative infrequency of normal bronchoscopic findings in this series and the rarity of the so-called typical allergic mucosa are self-evident. Exaggeration of the normal respiratory movements of varying degree was noted in 28 per cent of the cases. Collapse of the bronchial wall on coughing was a very frequent finding but apparently was not related to the character of movements during quiet respiration.

Composite Respiratory Tract Findings.—In Table III the cases have been classified on the basis of the combined findings of rhinological and bronchoscopic examination.

TABLE III. CLASSIFICATION OF UPPER AND LOWER RESPIRATORY TRACT FINDINGS

FINDINGS	NUMBER OF CASES	PER CENT
Chronic suppurative sinusitis and chronic suppurative bronchitis	65	26.0
Chronic suppurative sinusitis and chronic nonsuppurative bronchitis	50	20.0
Chronic suppurative sinusitis and normal bronchi	10	4.0
Negative sinuses and chronic suppurative bronchitis	48	19.2
Negative sinuses and chronic nonsuppurative bronchitis	42	16.8
Negative sinuses and normal bronchi	19	7.6
Chronic nonsuppurative sinusitis and chronic suppurative bronchitis	10	4.0
Chronic nonsuppurative sinusitis and chronic nonsuppurative bronchitis	5	2.0
Chronic nonsuppurative sinusitis and normal bronchi	1	0.4
Total	250	100.0

Analysis of Table III reveals that 183 patients in this series (73.2 per cent) had chronic respiratory tract infection: 26 per cent in both sinuses and bronchi, 24 per cent in the sinuses alone, and 23.2 per cent in the bronchi alone. As to correlation between infection in the sinuses and bronchi, it can be noted that in the 125 cases of chronic suppurative sinusitis, chronic bronchial infection was present in 52 per cent. In the 109 cases with no sinus infection, chronic bronchial infection occurred in 44 per cent. In the 123 cases of chronic suppurative bronchitis, chronic sinus infection was found in 52.9 per cent. In the remaining 127 cases without demonstrable bronchial infection, the incidence of sinus infection was 49 per cent. The difference of incidence in these comparable

groups of cases are not considered significant and do not evidence any relationship between the two infections.

ILLUSTRATIVE CASES

CASE 1.—A man, aged 24 years, gave a history of recurrent asthma since early childhood. The patient was transferred to England for overseas duty in October, 1943, and asthmatic attacks increased markedly in severity and frequency, requiring many epinephrine injections. General medical examination was negative except for persistent wheezing rhonchi throughout chest. An ear, nose, and throat consultant reported no evidence of chronic sinus disease but noted active nasal allergy. Allergy survey disclosed moderate skin reactions to inhalants and pollens. On bronchoscopy, membranes were found to be pale, swollen, and boggy, and secretions were clear, watery, and excessive. Respiratory movements were slightly exaggerated. Impression: allergic bronchitis.

This represents one of the few cases observed with the so-called typically appearing allergic bronchial mucosa.

CASE 2.—A man, aged 27 years, gave a history of wheezing and persistence of cough with winter colds for eight years. Four months after arrival in New Guinea, the patient developed recurrent wheezing and dyspnea of increasing severity. General medical examination was negative except for mild wheezing and rhonchi in chest. An ear, nose, and throat consultant reported moderate chronic suppurative infection in both ethmoids. Allergy survey disclosed a few moderately positive skin reactions to inhalants. On bronchoscopy, the mucosa was found to be mildly reddened and moderately thickened. Scattered viscid, tenacious, mucoid secretions, difficult to remove by suction, were noted. Impression: chronic nonsuppurative bronchitis of moderate degree.

This illustrates a case with chronic sinus infection and chronic bronchitis of the nonsuppurative or noninfectious type.

CASE 3.—A man, aged 24 years, gave a history of recurrent asthma since early childhood with attacks occurring several times weekly throughout the year. Hospitalization and frequent epinephrine injections were required for several severe relapses. Physical examination revealed restricted diaphragmatic movement and marked wheezing rhonchi throughout the chest. An ear, nose, and throat consultant found no evidence of chronic sinus disease. On allergy survey, markedly positive skin reactions to a number of inhalants and foods were obtained. Bronchoscopy revealed a thin, reddened mucosa and large amounts of thick purulent secretion in every subdivision of the bronchial tree. Impression: chronic suppurative bronchitis of severe degree.

This illustrates the occurrence of well-established chronic bronchial infection in a young asthmatic patient. In view of the negative sinuses and well-defined skin reactions to extrinsic allergens, this case might ordinarily have been regarded as one of simple extrinsic asthma.

CASE 4.—A man, aged 30 years, gave a history of nine months' duration of recurrent cough, wheezing, and dyspnea of increasing severity, beginning in New Guinea. Associated symptoms of frequent nasal obstruction, yellowish nasal discharge, and sneezing were present. General medical examination revealed evidence of nasal infection and persistent wheezing rhonchi throughout chest. An ear, nose, and throat consultant reported chronic, severe suppurative pansinusitis. On allergy survey, mildly positive skin reactions to several inhalants were noted. On bronchoscopy, the mucosa was found to be moderately reddened and thickened, and a moderate amount of mucopurulent secretion was noted throughout. Impression: chronic suppurative bronchitis of moderate degree. Cytologic studies of nasal secretion revealed 90 per cent neutrophiles and 3 per cent eosinophiles. Smear of bronchial secretion showed 60 per cent neutrophiles and 40 per cent lymphocytes.

This represents a case of asthma of relatively short duration in a young individual with well-established chronic infection in both upper and lower respiratory tracts. The primary etiological factors were probably intrinsic.

CASE 5.—A man, aged 21 years, gave a history of asthma since the age of 12, acute attacks at about monthly intervals and frequent interim wheezing, cough, and dyspnea. Physical examination revealed occasional wheezing rhonchi in chest. An ear, nose, and throat consultant reported chronic suppurative infection in all of the paranasal sinuses. On allergy survey, moderately positive skin reactions to feathers and dust were obtained. Bronchoscopy revealed the mucous membranes to be slightly reddened but not thickened. The secretions were mucoid in character and not increased in amount. Impression: normal bronchi.

This case illustrates the occurrence of advanced chronic sinus infection in an asthmatic patient with no significant evidence of bronchial pathology.

DISCUSSION

The only noteworthy finding disclosed by routine diagnostic studies in this series was the occurrence of chronic suppurative sinusitis or chronic sinus infection in 50 per cent of the patients. The reported incidences of chronic sinus disease in bronchial asthma, as cited by Tuft (26 to 82 per cent) and Urbach (12 to 89 per cent), show wide variation. Due to lack of classification of the sinus disease, the incidence of sinus infection is not determinable. In Leopold's study of 200 cases of asthma in soldiers returned from overseas, only one case of suppurative infection of the sinuses was demonstrated.

No report of an analogous survey of bronchoscopic findings in asthma could be found with which to compare our results. Andrews reviewed the literature and stated that only one of 399 cases of bronchial asthma had a normal tracheobronchial tree. As previously mentioned, he regarded the reported tracheobronchial changes as evidence of bronchitis; this was classified into four categories, but no account of their relative incidence was given. Tuft described the bronchoscopic findings in asthma in detail but was indefinite about their occurrence. The great majority (89.6 per cent) of our patients showed bronchoscopic abnormalities, interpreted as bronchitis, and our differentiation of types was somewhat similar to Andrews' classification. Since the bronchoscoped series was fairly varied and large, it afforded data for determining respective occurrence of these types.

The discovery of chronic bronchial infection in approximately one-half of the patients in this series was a surprise finding. Reflecting generally accepted opinion, Alexander[11] described chronic bronchial infection as a late complication of asthma, usually occurring in cases of long standing and in elderly individuals. In this series of predominantly young men, its incidence was common and apparently not related to duration of the asthma. Well-marked chronic bronchial infection was observed in this study in thirty cases of asthma of less than two years' duration. Of note was the finding of bronchial infection as commonly in the extrinsic as in the intrinsic types of asthma and its irrelation to chronic sinus infection. Asthmatic activity was more difficult to control in cases with bronchial infection, and the prognosis appeared unfavorable.

The exact nature of the bronchial pathology in the group with chronic nonsuppurative bronchitis could not be established with certainty. In some cases cytologic studies of secretions revealed eosinophiles as the predominant cells, indicating mainly allergic activity. In others the lymphocytes were increased

and predominant, suggesting a low-grade infectious process. The rarity of the "typical allergic mucosa" in the bronchi has been estimated by other observers.

One might inquire whether the recorded findings concerning complicating bronchitis in asthma could have been ascertained from examination of the sputum alone as suggested by Alexander. Sputum studies, in our series, did not yield satisfactory or comparable results.

The incidence of chronic respiratory tract infection in 73.2 per cent of the patients in this series is regarded as strikingly high. Only Hampton and Rand have reported findings approximating this figure. In their series of 286 cases of bronchial asthma, composed mostly of young soldiers, 49.2 per cent were considered to have chronic respiratory infection. These authors likewise direct attention to the frequent occurrence of respiratory infection in young asthmatic patients, and point out the belief of reliable authorities that this type of asthma was common only in individuals over 40 years of age.

The explanation for the recorded high incidence of chronic respiratory infection in bronchial asthma in soldiers remains to be determined. Their increased exposure to conditions disposing to respiratory infections is undoubtedly one of the important factors involved. One wonders also whether our diagnostic procedures were not more comprehensive than are ordinarily expedient in the examination of asthmatic patients and whether more instances of infection were uncovered on that account.

Authoritative opinions regarding the role of chronic respiratory infection in bronchial asthma vary considerably. It is quite generally agreed that such infection is of etiological importance both as a predisposing and causative factor in asthma. The exact causal relationships have been difficult to demonstrate and apparently constitute the chief bone of contention. Tuft mentioned chronic sinus infection as the most important of all focal infections in the etiology of asthma. Urbach gave more prominence to chronic bronchial infection but recorded no estimate of its comparative significance. Critical study of this problem in our individual cases was beyond the scope of our investigation. A few general observations are offered. (1) Chronic sinus infection was apparently instrumental in provoking the onset of asthma as well as maintaining its activity in a significant number of cases, both extrinsic and intrinsic. (2) Chronic bronchial infection seemed equally important in sustaining asthmatic activity, but its influence in initiating the disease was less conspicuous. (3) As others have mentioned, chronic respiratory infection appeared to have secondary aggravating effects on an established asthma as to therapy, generally speaking. We believe that the treatment of chronic sinus infection in bronchial asthma should be directed by a rhinologist. An adequate trial of conservative measures is urged before major operations are contemplated. Control of underlying nasal allergy is important but of secondary concern. Old time measures for the treatment of chronic bronchial infection do not seem adequate. Supplementary use of the new chemotherapeutic agents offer better prospects for cure. Administration of sulfonamides and penicillin did not prove sufficiently beneficial to warrant their general use. Topical application of sulfonamides and tyrothrycin has been reported upon favorably and merits further investigation.

SUMMARY

1. A survey of 250 cases of perennial bronchial asthma in soldiers, in whom routine diagnostic studies were supplemented by bronchoscopy, has been presented.

2. Of those cases, 81.4 per cent were medical casualties evacuated from overseas, 84 per cent were under 35 years of age, and 43.8 per cent had asthma of less than five years' duration.

3. Fifty per cent of the patients had chronic suppurative sinusitis.

4. Bronchoscopy revealed bronchial abnormalities in 89.6 per cent of the series. These were differentiated as (1) chronic suppurative bronchitis in 49.2 per cent; (2) chronic nonsuppurative bronchitis in 38.8 per cent; and (3) allergic bronchitis in 1.6 per cent.

5. Chronic bronchial infection was noted in a significant number of young individuals with asthma of relatively short duration.

6. In this series, chronic suppurative infection of the respiratory tract was found in 73.2 per cent of all patients.

7. The significance of this observed incidence of chronic respiratory infection in asthma has been briefly discussed.

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REFERENCES

1. Leopold, H. C.: Study of Asthmatics Returned From Overseas, J. ALLERGY **16**: 30, 1945.
2. Hampton, S. F., and Rand, H.: The Problem of Allergy at an Army Air Force's Hospital, J. ALLERGY **15**: 355, 1944.
3. Blank, P.: Military Aspects of Allergy, J. Lab. & Clin. Med. **28**: 609, 1943.
4. Alford, R. I.: The Disposition of Soldiers With Bronchial Asthma, J. ALLERGY **15**: 196, 1944.
5. Jackson, C.: Wheezing Respiration in Children, Am. J. Dis. Child. **41**: 153, 1931.
6. Clerf, L. H.: Present Status of Bronchoscopy in Bronchial Asthma, Ann. Int. Med. **9**: 1050, 1936.
7. Andrews, A. H.: Bronchoscopy in Bronchial Asthma, Illinois M. J. **73**: 25, 1938.
8. Tuft, L.: Clinical Allergy, Philadelphia, 1937, W. B. Saunders Co.
9. Feinberg, S. M., and Durham, O. C.: Allergy in Practice, Chicago, 1944, The Year Book Publishers, Inc.
10. Urbach, E., and Gottlieb, P. M.: Allergy, Philadelphia, 1943, Grune & Stratton.
11. Alexander, H. L.: Synopsis of Allergy, St. Louis, 1941, The C. V. Mosby Co.

ALLERGY IN THE PACIFIC

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THAT manifestations of allergy are on the increase in the Armed Forces can safely be stated after comparing statistics of the past with the present. In 1941, by including nasal polyps, headache, chronic bronchitis, hypertrophic rhinitis, and eczema as possible allergic conditions (although they are not specified as such in Naval vital statistics) there were only 1,035 cases of allergy admitted to Naval hospitals. There have been 500 cases admitted to the allergy service in this one hospital in the last six months. Hampton and Rand[31] diagnosed 921 cases of respiratory allergy and 327 cases of other allergic diseases at the Regional Hospital of the Army Air Forces of San Antonio Aviation Cadet Center, Texas, from Aug. 1, 1942, to Aug. 1, 1943.

Many individuals with dormant allergic potentialities suddenly find these becoming active when subjected to the stress and strain of military regimentation and combat duty.

The constancy of tropical climates, with lush vegetation, heavy rainfall, abundance of coral dust, fungi, insects, etc., tends to precipitate allergic reactions.

That there is a large psychogenic and neurogenic factor behind many of these allergic conditions, particularly urticaria, angioneurotic edema, allergic rhinitis, migraine, and asthma, cannot be doubted after nearly three years of observation and study of these conditions in members of the Armed Services. As stated by Ackerly,[1] "It is common knowledge that the body cannot put up the kind of fight in the presence of excessive mental tension and anxiety that it can without it." Rackemann,[2] in discussing asthma, stated that it is not always entirely allergic or entirely nervous; whereas there is a clear cut allergic group on one side and a small purely nervous group on the other, there are mixtures of all sorts in between.

There is little difference in allergy here than that found in the United States. There are no particular plants, molds, or fungi that are the precipitating causes in the majority of the cases. Psychogenic factors are pronounced but otherwise the general run of patients is about the same here as in the United States. One does not have here important sectional pollen problems, although Young, Cook, and Kawasaki[3] believe that, of the pollens which produce allergic rhinitis and asthma in Hawaii, the Algeroba tree is the most important, with pollens of grasses next in importance. The perpetuity of vegetation, occasioned by the lack of variation in seasons, permits almost constant pollination.

Many of the patients seen in this area came from stations where it is very dusty or very damp. Many of them mention the fact that the red volcanic dust or the gray coral dust tends to produce their symptoms. The dust seems to be merely a local irritant[4]; slides exposed to the atmosphere here have shown an

TABLE 1

	NUMBER OF PATIENTS	AVERAGE AGE (YR.)	AVERAGE DURATION OF ILLNESS (YR.)	FIRST SYMPTOMS IN THIS AREA (%)	EXAGGERATED SYMPTOMS IN THIS AREA (%)	OTHER ALLERGIC MANIFESTATIONS (%)	AVERAGE B.P.	AVERAGE W.B.C.	AVERAGE EOSIN. (%)	AFFECTED BY SEA (%)	ALLERGIC BACKGROUNDS (%)	PERENNIAL (%)	SEASONAL (%)	PSYCHOFACTOR (%)	RESPONSIVE TO SYMPTOM TREATMENT (%)	RESPONSIVE TO ELIMINATION DIET (%)	NUMBER RETURNED TO DUTY	NUMBER EVACUATED (%)
Asthma	58.60% 293	28	10	17.39	86.61	60.97	120/76	8,677	4	16.39	72.46	82.17	17.83	16.39	61.34	Not used	15.72	84.28
Hay fever	11.20% 56	25	9	35.71	64.29	80.35	118/76	6,887	3.5	10.71	69.64	67.97	32.03	21.42	23.21	12.5	82.15	17.85
Urticaria	7.60% 38	25	5	55.26	52.63	50	111/72	7,882	4	13.15	50	86.84	13.16	52.63	50	39.45	63.16	36.84
Allergic rhinitis	7% 35	29.5	9	22.85	77.15	82.85	115/75	7,233	3.5	11.42	60	88.58	11.42	25.71	31.42	17.14	80	20
Angioneurotic edema	3.20% 16	23	1.1	75	0	75	114/80	8,333	2.5	6.87	62.5	75	25	50	56.25	56.25	37.5	62.5
Migraine	2.60% 13	24	6	7.69	38.46	46.15	116/77	7,903	3.31	23.08	46.15	76.92	23.08	23.08	69.44	23.08	38.46	61.54
Allergic bronchitis	2.60% 13	36	15	23.08	76.92	69.44	115/79	9,211	3	0	46.15	84.62	15.38	7.69	38.46	0	46.15	53.85
Headache	2.20% 11	27	9	18.18	81.82	45.45	126/76	6,160	2.5	0	72.72	100	0	9.09	27.27	9.10	90.90	9.10
Allergic dermatitis	1.20% 6	27	2.5	33.33	66.67	50	119/68			0	66.67	66.67	33.33	0	50	50	83.33	16.67
Allergic conjunctivitis	0.80% 4	22.5	3.5	25	50	50	118/65			0	75	75	25	0	50	25	75	25
Histamine cephalgia	0.80% 4	29.5	9	50	50	100	124/81			0	75	100	0	25	50	50	75	25
Gastrointestinal allergy	0.80% 4	24	10	0	50	75	125/79	7,400	0	0	75	75	25	50	50	50	50	50
Tropical eosinophilia	0.80% 4	24	0.69	100	0	50	110/70	23,500	22.12	0	25	100	0	0	100		25	75
Physical allergy	0.60% 3	31	20	33.33	66.67	100	130/93	6,000	2	0	66.67	100	0	100	66.67	0	33.33	66.67

enormous amount of dust and very few pollen grains. Exposed agar petri plates demonstrated very little mold present in the air.

Dampness and rainy weather evidently play a leading role. The tendency for many allergic conditions to become exaggerated by close proximity to the sea, as has been emphasized by Rowe,[5] has been repeatedly observed in many cases. Many patients afflicted with allergic rhinitis, asthma, migraine, and urticaria, who have lived inland most of their lives, upon entering the Navy and thus having continuous contact with the sea atmosphere develop these allergic conditions in an exaggerated form. Peters[6] showed that, "among the nonspecific causes of bronchial asthma weather changes must be considered among the most important . . . there are patients [whose symptoms], without their knowledge, exactly follow the barometric pressure."

The system used in the diagnosis of allergic conditions in this branch of the service varies but little from that used in civilian practice. Considerable stress is placed on the history which is taken in a thorough manner and recorded on mimeographed forms. Skin tests are performed in assembly line style using local inhalants and dusts, mostly. Animal emanations and foods are used, also, more particularly where the history indicates such a sensitivity and when the offending allergens are vague and no definite clue is discernible.

Management of allergic conditions is carried out symptomatically by prescribing the more commonly recognized drugs for the treatment together with elimination diets and hyposensitization. However, the latter is used only when the patient will be able to continue this form of therapy for several months. Both subcutaneous and intradermal injections are given.

Dietary therapy, in a strictly supervised manner, is used exclusively in all forms of allergy except most cases of asthma. The diets used are usually those advocated by Rowe.[3,4]

The improvement shown by many of these patients on diet therapy, particularly those with allergic rhinitis and acute urticaria, has been gratifying.

From May 1 to Nov. 1, 1944, a total of five hundred cases was received on the allergy service of this Naval hospital with a diagnosis of some form of allergy. These cases have been broken down into tabular form and the results are recorded in Table I.

Of these 500 patients, 293 (58.60 per cent) had asthma; 56 (11.20 per cent) had hay fever; 38 (7.60 per cent) had urticaria; 35 (7 per cent) had allergic rhinitis; 16 (3.20 per cent) had angioneurotic edema; 13 (2.60 per cent) had migraine; 13 (2.60 per cent) had allergic bronchitis; 11 (2.20 per cent) had headaches of various types actuated by nasal obstructions, polyps in sinuses, nervous tension, sunlight, etc.; 6 (1.20 per cent) had allergic dermatitis; 4 (0.80 per cent) had allergic conjunctivitis; 4 (0.80 per cent) had histamine cephalgia; 4 (0.80 per cent) had tropical eosinophilia; and 3 (0.60 per cent) had physical allergy.

The average age for the whole group was 27.6 years. The average duration of the illness was eight years. Thirty-five per cent had their initial symptoms in this area, and 64 per cent showed, here, an exaggerated phase of their al-

lergic condition. Out of 500 recorded cases, 347 knew some precipitating factor which would activate their condition. The average blood pressure was 118/77. The average white blood count was 9,014, with an average eosinophile count of 5 per cent. A few (13 per cent) showed exaggeration of their symptoms when in close proximity to the sea; 66.80 per cent had multiple allergic manifestations; 61.42 per cent had an allergic background; and 84.34 per cent of these manifestations were perennial while 15.66 per cent were seasonal in character. Some (34 per cent) acknowledged that emotional factors would precipitate attacks. Signs of emotional instability, such as fingernail biting, increased perspiration, cold, wet, clammy hands, etc., were not included in this percentage. In 48 per cent, there was no response to symptomatic therapy; but the other 52 per cent did respond, and in 33 per cent this could be attributed to dietary management. A small majority (56 per cent) of the 500 patients were returned to duty, whereas 44 per cent were evacuated to the mainland as not fit for duty in the combat area.

In the series reported by Hampton and Rand,[31] three-fourths of the patients had respiratory allergies. Of the author's cases, 79 per cent, including those with allergic rhinitis, were respiratory in character. Of a total of 1,310 patients with allergy seen in 1942 by Gold and Bazemore[32] in an Army Allergy Section, 51 per cent had asthma; 11.38 per cent had hay fever; 3.5 per cent had allergic rhinitis; 9.16 per cent had urticaria and angioneurotic edema; 0.99 per cent had migraine; and 0.15 per cent had gastrointestinal allergy. This compares favorably with the cases seen in this area, with the exception that the percentage of asthma here was a little higher. Young and his co-workers[3] found asthma and allergic rhinitis to be more severe in Hawaii than on the mainland. A comparison of the statistics given verifies this. Of Alford's[2] cases of asthma, 71 per cent were discharged, and 29 per cent were returned to limited duty. Among the cases seen in this area, 16 per cent were returned to duty, and 84 per cent were evacuated. The criteria used here in returning a confirmed asthmatic or other allergic patient to duty were based upon the character of the work he performed and the severity of symptoms. If he was performing clerical work or some type of sedentary effort where he was not exposed to the elements, in many instances it was found that he would be able to carry on. On the other hand, if his duty was such that he might be called into actual combat he was determined as unfit for the service.

Of Alford's cases, 23 per cent had their initial attack overseas. Of the cases cited in our own correlation 17 per cent had their first attack in this area.

Table I, a statistical analysis, is self-explanatory.

MISCELLANEOUS ALLERGIES

Penicillin Allergy.—Feinberg[7] states that 6 per cent of allergic persons are sensitive to the antigen of the *Penicillium* group and that 11 per cent of the fungus spores in the air in the Midwestern United States are *Penicillium* spores.

Lyons[8] found reactions analogous to serum sickness, mainly urticaria, in 5.7 per cent of his cases receiving penicillin but stated that the period of sensitization was temporary and that it was not necessary to discontinue this form of

therapy because of such reactions. Denny and his associates[9] found no urticaria in his series but noted contact dermatitis, dizziness, and headache in patients receiving penicillin. Criep,[10] using direct skin tests with *Penicillium* extract, found negative reactions. This is of interest because of the fact that Feinberg's tests showed that persons clinically sensitive to *Penicillium* spores did *not* react to penicillin. This would indicate that there is no cross sensitization between the penicillin drug and *Penicillium* spore extract and that the allergic reaction is not unlike that of a serum allergy.

In the past two years it has been the author's privilege to observe this preparation administered to hundreds of men, intravenously, intramuscularly, in body cavities, and topically. These observations were made in three large Naval establishments located in widely separated areas. The pathologic circumstances ranged from acute to mild ambulatory cases; all patients were suffering from variable diseases and infections. In none of these cases was there any marked local or systemic reaction that would indicate a severe allergic condition. There were a few transitory irritations of veins on prolonged intravenous administration. There were a few mild urticarial reactions and an occasional moderate elevation of temperature, but in no instance was the preparation discontinued because of these reactions.

Sulfonamide Allergy.—Gessler[14] believes that minor reactions from sulfonamide are due to allergic or pharmacologic reactions and that kidney damage and hematuria are due to a mechanical factor. Major reactions such as focal necrosis, agranulocytosis, and periarteritis nodosa may be due to a combination of these factors.

Long[15] found that ten to fifteen million people received at least one of the sulfonamides during the year 1941. He warned of the possibility of sensitization to these drugs. In his series of cases showing reactions to sulfonamides, sulfanilamide produced 11.9 per cent reactions; sulfapyridine, 15.9 per cent; sulfathiazole, 18.6 per cent; and sulfadizine, 6.5 per cent.

Dowling and his associates[16] found more calculi, fever, dermatitis, and conjunctivitis with sulfamerazine than with sulfadiazine.

Bunting and Levan[17] administered sulfaguanidine to 191 carriers of bacillary dysentery and noted febrile reactions in eighteen of their patients. Five developed dermatologic reactions. Twenty per cent developed other manifestations attributed to the drug. Eleven and one-half per cent developed complications severe enough to warrant discontinuance of the drug.

Lee[18] gave 2 Gm. of sulfadiazine to 25,000 persons as a prophylactic against pneumococcic, streptococcic, and meningococcic infections and noted reactions in 128 cases.

Large amounts of the sulfonamides are used in military medicine. No definite figures are available as to systemic reactions. However, since sulfanilamide, sulfapyridine and sulfathiazole have been replaced largely by the more soluble and less toxic sulfadiazine, it can safely be said that some of the figures given have been very appreciably modified.

Blood Plasma Allergy.—The enormous amount of pooled plasma used both by civilian practitioners and by military physicians and corpsmen warrants the

reiteration of the possibility of an allergic response to this type of therapy. More particularly is this true in the combat areas.

Colonnell[29] reported a case of ragweed sensitivity introduced by whole blood transfusion. This was augmented later by a marked allergic reaction following a subsequent administration of pooled blood plasma that contained ragweed antigen.

Strumia, McGraw, and Blake[30] have stressed the allergic possibility of parenteral administrations of plasma and blood.

Fortunately, the incidence of such reactions is very low.

Tropical Eosinophilia—an Allergic Condition.—A disease of unknown etiology, which has asthmatic signs and symptoms and also an extremely high eosinophilia, has been described and named "tropical eosinophilia" by Weingarten.[19]

Other authors have described chest conditions associated with high eosinophile counts. Loeffler[20] reported similar cases to which he gave the term "transient pulmonary infiltration with eosinophilia."

Emerson,[21] in India, described a case with asthmatic signs and symptoms and a 78 per cent eosinophilia. Scherlis,[22] in California, reported a case of eosinophilic pneumonia with an eosinophile blood count of 33 per cent. Loeffler[20] suggested that the syndrome was an allergic manifestation.

Epidemic bronchial asthma or "Guhu" has been included in the health reports of Mashita and Homma,[23] from Micronesia. In 1923, their reports from Saipan stated that bronchial asthma was prevalent among the children there.

Asthma due to *Ascarias* has been reported from Guam, Samoa, and the West Indies, but no mention was made of the eosinophile count. Slowly[24] reporting a case of "Transient Successive Pulmonary Infiltration (Loeffler's Syndrome)" associated with trichiniasis, cites Young and Kline's reversible allergic reaction in bronchial and interstitial tissues in asthma as evidence that Loeffler's syndrome is a definite allergic response.

Allen[25] points out that eosinophilia is occurring in increasing numbers among the Armed Forces in the Southwest Pacific area. He states that hookworm infection is the causative factor in most instances. Sixteen of his patients had eosinophile counts of 50 per cent while only eight of the sixteen showed hookworm ova in the stool. No mention was made of the admission diagnosis, symptoms, or physical findings.

During the past several months four patients who could be classed under tropical eosinophilia have been treated in this hospital. These met the specifications of Loeffler's syndrome as elicited from the history recorded in the health record or as found at the time of admission examination. That is, they showed signs of pulmonary disease by percussion and auscultation. Changes in the lung tissue were revealed by x-ray examination. There were also a transience of the pulmonary signs and an extremely high eosinophile blood count. These patients all had repeatedly shown negative stool examinations for ova and parasites. Muscle biopsies for trichiniosis were negative. They all had the cardinal signs, symptoms, and physical findings of asthma. These were relieved by the admin-

istration of epinephrine. All responded to arsenical therapy as revealed by alleviation of their symptoms and a marked reduction in the eosinophile blood count.

All four patients had duty in the Southwest Pacific. One was in Shanghai, but none of the others had touched the mainland of Asia. All had been in New Zealand, Samoa, and Wallis Islands. With the exception of one, their symptoms dated back several months. They had had an acute onset resembling upper respiratory infection accompanied by dyspnea, cough, fever, and a persistance of dyspnea after all other symptoms had subsided. Two gave a history with an allergic background. One man had a previous history of asthmatic symptoms, and one gave a history of having had hay fever.

Skin tests for intestinal parasites, filariasis, and inhalants were negative, as also were the stool examinations and the muscle biopsies. The average white blood count was 18,500 with an average eosinophile count of 59 per cent. No other known conditions reveal such a high eosinophile count with the exception of trichinosis, periarteritis nodosa, eosinophilic leucemia, and rarely, Hodgkin's disease.

The consensus of most authors on this rare condition is that it is an allergic response to a protozoan infection since it responds to arsenical therapy, and also because the lungs are the shock tissue most frequently affected. "For the present it may be assumed that Loeffler's syndrome is an allergic reaction that can be provoked by a variety of allergens. The relationship of tropical eosinophilia to Loeffler's syndrome is not clear—the two conditions are similar and are not clearly distinguishable."[33]

No signs or symptoms of a parasitic infection were found in any of the cases seen in this area. In many of the cases of tropical eosinophilia reported in the literature herein quoted the presence of parasitic infection was not mentioned.

The 81 patients in Weingarten's[19] series were all in the vicinity of the seacoast around Bombay, India. The patients seen in this area had been in New Zealand, Samoa, and some of the islands of the Southwest Pacific. One had been in China.

This observation is cited because this condition has been observed in our troops which have not been in the vicinity of India. This may indicate that the incidence of this condition may be more prevalent and more widespread than was heretofore believed. Thus, it will have to be considered in those cases of presumably intrinsic asthma accompanied by a high eosinophile blood count.

Filiariasis—A Possible Allergic Reaction.—A tropical disease of extreme importance in military medicine, particularly relative to the Naval and Marine personnel, is the nematode infection, filiariasis. This is becoming recognized as a possible allergic reaction rather than wholly infectious in character.

Outstanding characteristics of this condition are its transitory nature and its frequency of recurrence. Fogel and Huntington[26] described genital manifestations of this condition as, "the more diffuse transient lymphangitis. Presumably a sensitization phenomenon due to a diffusable agent released from a worm which may be some distance from the lesion."

O'Conner[27] called this edema "fugitive swelling."

Michael[28] studying the histologic aspects of this phenomenon in this hospital and also on the West Coast came to the following conclusions:

Cultures of numerous cases showed the lymphangitis not to be of infectious origin as found in most instances, but rather to have all the earmarks of an allergic response. In other words, there was found a marked infiltration of eosinophiles around the living worm, accompanied by edema, vascular engorgement, and a round cell infiltration.

This same histopathologic picture was found in areas where the worms were not present. This indicates an allergic reaction due to a diffusible agent produced by the parasite in more distant areas of the body.

Fogel[26] aspirated fluid from hydroceles of persons afflicted with this condition and found no microfilariae. However, the fluid showed numerous eosinophiles. The allergic nature of this condition is further verified by intradermal skin tests, using *Dirofilaria immitis* antigen. This method first was used by Huntington, who prepared the antigen from parasites obtained from Samoan dogs. This antigen gives both an immediate and a delayed skin reaction. Also it incites pain, tenderness, swelling, and redness in the glands and other regions originally affected. In 137 cases of Mumo (a native term used by Buxton to describe the clinical entity of filiariasis) Huntington found that 83.1 per cent of the patients gave positive skin reactions. Michael,[28] using the same type of antigen, found 87.3 per cent positive reactions.

In this hospital during the past several months, hundreds of young men have been observed with filiariasis.

The transitory edema, skin manifestations simulating erythema multiforme and urticaria, eosinophilic infiltration at the site of the affected area without demonstration of the worm, an increase of eosinophiles in the blood count (rarely over 10 per cent), the presence of eosinophiles locally, and the absence of microfilariae in the aspirated fluid would seem to emphasize that this condition may be an allergic reaction.

SUMMARY

1. There is an apparent increase in allergic conditions in the Armed Forces.

2. Psychogenic factors play a prominent role in allergic conditions in military life.

3. There is very little difference in the allergic conditions observed in the Pacific area as compared with those seen on the continental United States.

4. Five hundred cases of allergy seen in this area were studied and the findings are herein tabulated.

5. Penicillin allergy, at most, was found to be mild.

6. The toxic manifestations of sulfonamides must be considered when these drugs are administered.

7. Allergic reactions from blood plasma are rare, but may occur in potentially allergic individuals.

8. Tropical eosinophilia and Loeffler's syndrome may be more widespread than was previously thought to be the case. They must be considered in cases of asthma with high eosinophile counts.

9. Filiariasis is probably a tropical disease with a strong allergic reaction and must be considered in making a differential diagnosis between atypical urticaria, angioneurotic edema, and the Arthus phenomenon.

REFERENCES

1. Ackerly, S.: Is There an Anxiety Component to Every Complaint? South. M. J. 37: 287, 1944.
2. Alford, R. T.: The Disposition of Soldiers With Bronchial Asthma, J. ALLERGY 15: 196, 1944.
3. Young, C. T., Cook, W. R., and Kawasaki, I. A.: Allergic Rhinitis and Asthma in Hawaii, War Med. 3: 282, 1943.
4. Blue, J. A.: Dust—Its Effects on Man From a Medical Standpoint, South. M. J. 31: 1101, 1938.
5. Rowe, A.: Seasonal and Geographic Influences on Food Allergy, J. ALLERGY 13: 55, 1941.
6. Peters, J.: Status Asthmaticus, Illinois M. J. 82: 428, 1942.
7. Feinberg, S. M.: Penicillin Allergy, J. ALLERGY 15: 271, 1944.
8. Lyons, C.: Penicillin Therapy of Surgical Infections in U. S. Army, J. A. M. A. 123: 1008, 1943.
9. Denny, E. R., Shallenberger, P. L., and Pyle, H. D.: Clinical Observations in the Use of Penicillin, J. Oklahoma M. A. 37: 193, 1944.
10. Criep, L. H.: Allergy to Penicillin, J. A. M. A. 126: 429, 1944.
11. Goldman, L.: Some General Remarks on the Prevention of Irritation and Sensitization of the Skin to Chemical Compounds, South. M. J. 37: 290, 1944.
12. Medical Manual of Chemical Warfare, revised edition, 1943, p. 8.
13. Davis, M. I. J.: The Dermatologic Aspects of the Visicant War Gases, J. A. M. A. 126: 209, 1944.
14. Gessler, C. N.: Deaths From Sulfonamides, South. M. J. 37: 365, 1944.
15. Blue, J. A.: Allergic Agranulocytosis, Am. J. M. Sc. 207: 453, 1944.
16. Dowling, H. F., Lepper, M. H., Dumoff-Stanley, E., and Sweet, L. K.: Relative Toxicity of Sulfamerazine and Sulfadiazine, J. A. M. A. 125: 103, 1944.
17. Bunting, J. J., and Levan, N. E.: Toxic Reactions of Sulfaguanidine Therapy, J. A. M. A. 125: 773, 1944.
18. Lee, R. V.: Reactions Following Mass Administration of Sulfadiazine, J. A. M. A. 126: 630, 1944.
19. Weingarten, R. J.: Tropical Eosinophilia, Lancet 1: 103, 1943.
20. Loeffler, W.: Transient Pulmonary Infiltration With Eosinophilia, Beitr. z. Klin. d. Tuberk. 79: 368, 1932.
21. Emerson, K., Jr.: Tropical Eosinophilia, U. S. Nav. M. Bull. 42: 118, 1944.
22. Scherlis, S.: Eosinophilia Pneumonia, Bull. U. S. Army M. Dept. 77: 27, 1944.
23. Mashita and Homa: U. S. Nav. Med. Bull. 42: 211, 1944.
24. Slowly, J. F.: A Case of Transient Successive Pulmonary Infiltration (Loeffler's Syndrome) Associated with Trichiniosis, Ann. Int. Med. 21: 130, 1944.
25. Allen, H. C.: Eosinophilia in the South West Pacific, U. S. Nav. M. Bull. 42: 1241, 1944.
26. Fogel, R. H., and Huntington, R. W., Jr.: Genital Manifestations of Early Filariasis, U. S. Nav. Med. Bull. 43: 263, 1944.
27. O'Conner, F. W., and Hulse, C. R.: Studies in Filiariasis in Puerto Rico, Puerto Rico J. Pub. Health & Trop. Med. 11: 167, 1935.
28. Michael, P.: Filiariasis Among Navy and Marine Personnel, U. S. Nav. Med. Bull. 42: 1059, 1944.
29. Colonnell, W. J.: Allergic Reactions to Plasma Transfusions, U. S. Nav. M. Bull. 41: 1356, 1943.
30. Bumed News Letters: Intravenous Fluids, Reactions, 2: 4, 1943.
31. Hampton, S. F., and Rand, H.: The Problem of Allergy at an Army Air Forces Hospital, J. ALLERGY 15: 355, 1944.
32. Gold, E. M., and Bazemore, J. M.: The Significance of Allergy in Military Medicine, J. ALLERGY 15: 279, 1944.
33. Editorial: Transitory Pulmonary Infiltration Associated With Eosinophilia, Loeffler's Syndrome, J. A. M. A. 126: 837, 1944.
34. Rowe, A. H.: Elimination Diets and the Patient's Allergies, Philadelphia, 1941, Lea & Febiger.

ETHYL-NOR-EPINEPHRINE BY INHALATION FOR BRONCHIAL ASTHMA; A COMPARISON WITH EPINEPHRINE

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SINCE the use of 1 per cent epinephrine by direct inhalation was described by Graeser,[3] it has been extensively used but has proved to be a mixed blessing. In the hands of well-informed physicians with a knowledge of the pathologic physiology involved in asthma and the pharmacology of epinephrine, this drug, by inhalation, has been a useful aid. Under the supervision of relatively uninformed physicians and pharmacists or under the self-supervision of totally uninformed laymen it has been productive of little good and some harm.

The adverse effects stem from two sources: (A) The local vasoconstrictor effect on mucous membranes, resulting in dryness, increased susceptibility to infection, ulceration, and gangrene. In this category belong cases of acute and chronic ulceration of the lymphoid nodules of the oral pharynx, ulceration of the tonsils, acute and chronic laryngitis, and ulceration of the vocal cords and other structures of the larynx. Changes in the trachea and main bronchi are rarer. (B) The effects due to overdosage. It is commonly forgotten that epinephrine for inhalation is ten times stronger than that for injection. Whether the inhaled material gets to the bronchioles or not, most of it is eventually absorbed. Assuming complete absorption, 0.05 c.c. or one drop by inhalation is equivalent to 0.5 c.c. of a 1:1,000 solution (the usual dose) by injection. One frequently sees patients (and hears stories of others) who have used 10 to 12 drops at one inhalation and 3 c.c. (equivalent to 30 c.c. of epinephrine, 1:1,000, by injection) during one night. They did not realize that, if a therapeutic dose did not afford relief, they may have been refractory to the drug. Instead of relief from wheezing they had tachycardia, tremor, headache, nausea, and other toxic effects. The margin between therapeutic and toxic doses of epinephrine is relatively small.

The author and his associates previously reported on the pharmacology and parenteral use in asthma of a new sympathomimetic drug, ethyl-nor-epinephrine.[1*] Chemically, it is 1-(3,4-dihydroxyphenyl)-2-amino-1-butanol. To recapitulate briefly, when injected intramuscularly or subcutaneously in approximately twice the dosage employed with epinephrine, it gave equivalent relief in uncomplicated extrinsic asthma.[2] In asthma with bronchial infection it was less efficacious than epinephrine.[2] ENE lacked the pressor effect of epinephrine; actually the diastolic pressure was moderately lowered, with a widening of the pulse pressure and slight acceleration of the heart rate. ENE did not provoke nausea and vomiting; this made it preferable for use in children. No angina was pro-

*For convenience the abbreviation "ENE" for ethyl-nor-epinephrine will be used hereafter.

TABLE I. COMPARATIVE RESULTS OF ENE AND EPINEPHRINE BY INHALATION IN TWENTY-EIGHT CASES OF UNCOMPLICATED EXTRINSIC ASTHMA

AGE OF PATIENT (YR.)	DRUG USED	SPEED OF RELIEF	DEGREE OF RELIEF	TREMOR	NERVOUSNESS	NAUSEA	TACHYCARDIA	ANGINA	PRESSOR EFFECT	LOCAL EFFECTS ON UPPER RESPIRATORY TRACT (AND PSYCHOTIC REACTIONS)
7	E	4	4	–	–	–	–	–	–	None
	B	4	4	–	–	–	–	–	–	None
9	E	4	4	–	–	–	–	–	–	None
	B	4	4	–	–	–	–	–	–	None
9	E	3	3	*	*	*	–	–	–	Manic reaction; no local
	B	4	2	–	*	–	–	–	–	None
10	E	4	4	–	–	–	–	–	–	None
	B	2	4	–	–	–	–	–	–	None
11	E	4	4	–	–	–	–	–	–	Recurrent ulceration of tonsils
	B	3	4	–	–	–	–	–	–	No local effects
12	E	4	4	–	–	–	*	–	–	None
	B	4	3	–	–	–	–	–	–	None
16	E	3	3	–	–	–	–	–	*	None
	B	4	4	–	–	–	–	–	–	None
21	E	3	3	–	–	*	–	–	–	None
	B	1	1	–	–	–	Sl	–	–	None
24	E	4	4	–	–	–	–	–	–	None
	B	4	4	–	–	–	–	–	–	None
25	E	3	4	–	–	–	–	–	–	None
	B	0	0	–	–	–	–	–	–	None
27	E	4	4	*	*	–	–	–	*	Chronic ulcerative pharyngitis
	B	4	4	–	–	–	–	–	–	Cleared up under ENE
27	E	2	3	–	–	*	–	–	–	None
	B	2	1	–	–	–	–	–	–	None
29	E	3	3	–	–	–	–	–	–	None
	B	1	2	–	–	–	–	–	–	None
31	E	4	4	*	*	–	–	–	–	None
	B	4	4	–	*	–	–	–	–	None
31	E	2	2	–	–	–	–	–	–	Recurrent ulceration of tonsils
	B	3	3	–	–	–	Sl	–	–	No ulceration from ENE
33	E	4	4	–	–	–	–	–	–	None
	B	4	4	–	–	–	–	–	–	None
34	E	3	3	–	–	–	–	–	–	None
	B	0	0	–	–	–	–	–	–	None
35	E	4	4	–	–	–	–	–	–	None
	B	1	1	–	–	–	–	–	–	None
38	E	3	2	*	*	–	–	*	*	Chronic laryngitis– 3 months
	B	2	3	–	–	–	–	–	–	Cleared up in 2 days
38	E	4	4	–	–	–	Sl	–	–	None
	B	4	4	–	–	–	–	–	–	None
40	E	4	4	–	–	–	–	–	–	None
	B	3	4	–	–	–	–	–	–	None
43	E	2	2	–	–	*	–	–	–	None
	B	2	2	–	–	–	–	–	–	None
45	E	4	4	–	–	–	–	–	–	None
	B	4	4	–	–	–	–	–	–	None
50	E	2	2	–	*	–	–	*	–	None
	B	2	1	–	–	–	–	–	–	None
51	E	4	4	–	–	–	–	–	–	None
	B	3	2	–	–	–	–	–	–	None
56	E	2	2	*	*	–	*	*	*	Ulcerative laryngitis– 5 weeks
	B	2	2	–	–	–	–	–	–	Cleared up in 4 days
60	E	4	4	–	–	–	–	–	–	None
	B	4	4	–	–	–	–	–	–	None
63	E	3	3	–	–	–	–	–	–	None
	B	3	4	–	–	–	–	–	–	None

E = Epinephrine B = ENE Sl = slight

duced in patients with associated cardiac or hypertensive disease; this made it preferable in this group. Finally, tremor and nervousness in general were encountered less with ENE than with epinephrine. Clinical trial of ENE by the inhalation method in these two general types of asthma was the next logical step.

METHOD

Since it was found that a solution of ENE, 1:500, was equivalent to 1:1,000 epinephrine by injection, in this study a 2 per cent solution of ENE was used in the inhalation studies for comparison with the effect of 1 per cent epinephrine. The same makes of nebulizers were used, or the very same nebulizers, thoroughly cleaned between drug changes. The cases selected were ones in which the effects, both good and bad, of epinephrine by inhalation were already known. The patient was told to use the same number of deep inhalations, two to four.

TABLE II. COMPARATIVE RESULTS OF ENE AND EPINEPHRINE BY INHALATION IN FOURTEEN CASES OF ASTHMA WITH BRONCHIAL INFECTION

AGE OF PATIENT (YRS.)	DRUG USED	SPEED OF RELIEF	DEGREE OF RELIEF	TREMOR	NERVOUSNESS	NAUSEA	TACHYCARDIA	ANGINA	PRESSOR EFFECT	LOCAL EFFECTS ON UPPER RESPIRATORY TRACT
18	E	4	4	–	–	–	–	–	–	None
	B	4	4	–	–	–	–	–	–	None
19	E	3	3	–	–	–	*	–	–	Chronic laryngotracheitis
	B	2	2	–	–	–	–	–	–	Cleared on changing to ENE
24	E	2	2	*	*	*	*	–	–	None
	B	0	0	–	–	–	–	–	–	None
26	E	3	3	–	–	–	–	–	*	None
	B	1	1	–	–	–	–	–	–	None
29	E	4	4	–	–	–	–	–	–	Recurrent pharyngeal ulceration
	B	4	4	–	–	–	–	–	–	Freedom from ulcers
33	E	2	3	–	–	–	–	–	–	None
	B	1	1	–	–	–	–	–	–	None
39	E	4	3	*	*	–	*	–	–	None
	B	2	2	*	*	–	*	–	–	None
43	E	2	2	–	–	–	–	–	–	None
	B	0	0	–	–	–	–	–	–	None
44	E	4	4	–	–	–	–	–	–	Recurrent acute laryngotracheitis
	B	4	4	–	–	–	–	–	–	No recurrence under ENE
52	E	3	3	–	–	–	–	–	–	None
	B	0	0	–	–	–	–	–	–	None
54	E	1	1	*	*	*	–	*	–	None
	B	0	0	–	–	–	–	–	–	None
55	E	4	4	–	–	–	–	–	–	None
	B	3	3	–	–	–	–	–	–	None
60	E	4	4	–	*	–	–	*	*	Ulcerated vocal cords—hoarseness
	B	3	3	–	–	–	–	–	–	Clearance on change to ENE
66	E	4	4	–	–	–	–	–	–	None
	B	0	0	–	–	–	–	–	–	None

E = Epinephrine B = ENE

RESULTS

Table I shows the results obtained in uncomplicated extrinsic asthma, Table II shows those obtained in asthma complicated by bronchial infection, and Table III gives a summary of the observations in both groups. Speed of relief is noted on a scale from "0" (absent) to "4" (maximum). Otherwise they are noted "–" for absent or "*" for present.

TABLE III. SUMMARY OF OBSERVATIONS

NUMBER OF CASES	28 CASES		14 CASES	
TYPE OF ASTHMA	UNCOMPLICATED EXTRINSIC ASTHMA		ASTHMA WITH BRONCHIAL INFECTION	
DRUG USED	EPINEPHRINE TREATED	ENE TREATED	EPINEPHRINE TREATED	ENE TREATED
SPEED OF RELIEF				
Rapid (4* and 3*)	23	17	10	5
Slow (2* and 1*)	5	9	4	4
None	0	2	0	5
DEGREE OF RELIEF				
High (4* and 3*)	23	17	11	5
Partial (2* and 1*)	5	9	3	4
None	0	2	0	5
NUMBER RELIEVED	28 (100%)	26 (93%)	14 (100%)	9 (64%)
NUMBER OF FAILURES	0 (0%)	2 (7%)	0 (0%)	5 (36%)
UNDESIRABLE LOCAL EFFECTS ON UPPER RESPIRATORY TRACT	5	0	4	0
SYSTEMIC SIDE EFFECTS				
Tremor	5	0	3	1
Nervousness	6	2	4	1
Nausea	4	0	2	0
Tachycardia	3	2	3	1
Angina	3	0	2	0
Rise in Blood Pressure	3	0	2	0
Mania	1	0	0	0

TABLE IV. RELATIVE IMPORTANCE OF ENE AND EPINEPHRINE ON MECHANISMS INVOLVED

LUMEN-INCREASING EFFECT	EFFECT POSSESSED BY EPINEPHRINE	EFFECT POSSESSED BY ENE	RELATIVE IMPORTANCE OF EFFECT IN UNCOMPLICATED EXTRINSIC AND REFLEX ASTHMA	RELATIVE IMPORTANCE OF EFFECT IN ASTHMA WITH BRONCHIAL INFECTION
1. Relaxation of bronchiolar smooth muscle spasm	*	*	* * * *	* * *
2. Lessening of mucosal edema due to improved lymphatic drainage allowed by relaxation of bronchospasm	*	*	* * *	* *
3. Lessening of vascular bed mucosa through vasoconstriction	*	–	* *	* * *
4. Lessening of mucosal edema by diminution the arteriolar-venule pressure differential	*	–	* *	* *
5. Lessening of secretion indirectly through constriction of vessels supplying mucous glands and epithelium	*	–	*	* * *

* = present
– = absent

COMMENT

An analysis of results requires a consideration of the mechanisms of action of these two drugs in the two types of asthma. These are summarized in Table IV. In "pure" or uncomplicated asthma the relaxation of bronchospasm and the lessening of edema through the improved lymphatic drainage are accomplished equally well by both medications. Epinephrine has the advantage of vasoconstriction on surface application which calls forth the other lumen-increasing factors shown. These initial effects due to vasoconstriction give more speedy relief also. However, that same vasoconstriction of epinephrine slows its absorption through the mucous membrane and delays the bronchodilator effect. ENE, because of its lack of vasoconstrictor power, does not have this initial antiedema and antisecretory effect of epinephrine, but it apparently arrives more rapidly at the myoneural junctions of the bronchiolar smooth muscle cells. The effects are, therefore, approximately equal in uncomplicated extrinsic asthma. In asthma complicated by bronchitis or secondary to it, however, the congestion, edema, and mucous production are significant factors upon which ENE has little or no effect. Hence in this type it is not surprising that it should fail entirely in some instances and, in general, be less effective than epinephrine.

In another series of eighteen cases, all of which responded to ENE, all were found to respond to epinephrine. This series was not studied as carefully as the previous one, the only object being to see if there were any cases relieved by ENE which epinephrine failed to relieve. The results of both series showed that ENE is not apt to be effective by inhalation if epinephrine is not.

Theoretically, when used by the inhalation method for the relief of asthma, neither of these drugs should cause any undesirable systemic actions. We would like to conceive of a minimum amount of the drug applied at the point of maximum effectiveness. Actually, however, the rate of absorption by this method is unpredictable, and the impatient asthmatic patient, laboring for his breath, is prone to disregard instructions. The more desperate or more unintelligent he is, the more he will use his own judgment. Strictly speaking, significant nausea, nervousness, tremor, tachycardia, pressor effect, or angina by this method should properly be regarded as signs of overdosage or toxic effects. To be realistic, however, we have to regard any actions accompanying the dose of inhaled drug that the patient deems necessary to relieve his asthma as side effects, undesirable but more or less inevitable.

In the analysis of these effects, systemic and local, the first notable feature is the lack of angina, nausea, and pressor effect in the ENE series. The second feature is the greatly lessened incidence and severity of tachycardia, tremor, and nervousness in the ENE series. Third, and of great importance, is the lack of unwanted local effect on the upper respiratory tract mucous membrane when using ENE.

Whether to prescribe ENE or epinephrine by inhalation, then, depends upon the type of asthma, the expected frequency of use, the intelligence of the patient, the frequency of supervisory medical consultation, and the incidence and type

of side reactions. Both drugs have their advantages and disadvantages, and there is a limited field for the supervised use of each.

SUMMARY

1. In uncomplicated asthma of extrinsic origin 2 per cent ENE is almost as effective as 1 per cent epinephrine by inhalation, their bronchodilator powers being equal.

2. In asthma complicated by bronchial infection epinephrine is definitely more effective than ENE, presumably because of its additional vasoconstrictor action.

3. Undesirable local effects on the upper respiratory tract encountered so frequently with epinephrine do not occur with ENE.

4. Toxic effects from inhalation of ENE are rare and minimal; those effects from epinephrine inhalation are frequent and often serious.

5. Choice of medication depends on several enumerated factors.

The ENE used in these investigations was supplied through the courtesy of the Winthrop Chemical Company.

REFERENCES

1. Tainter, M. L., Cameron, W. M., Whitsell, L. J., and Hartman, M. M.: Clinical Actions of Ethylnorsuprarenin, J. Pharmacol. & Exper. Therap. 81: 269, 1944.
2. Hartman, M. M.: Parenteral Use of Butanefrine in Asthma; A Comparison With Epinephrine, Ann. Allergy 3: No. 5, 1945.
3. Graeser, J. B.: Inhalation of Epinephrine Hydrochloride for Relief of Asthmatic Symptoms, J. ALLERGY 6: 415, 1935.

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CONTACT DERMATITIS DUE TO ACE ADHERENT

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AN INFREQUENT complication in the treatment of amputees has been dermatitis resulting from the use of "Ace Adherent." This preparation has been employed to obtain skin traction. From a group of several hundred amputees four cases of dermatitis traceable to "Ace Adherent" were observed. The essentials of one of these cases is given.

CASE REPORT

M. T., an American soldier, aged 24 years, was first seen in April, 1945. He was admitted to the hospital for the treatment of bilateral arm amputation and perforation of the right eyeball. After preliminary operation on both arms he was referred to an amputation center for further care. During his stay there his upper limbs were prepared for revision. During this preparatory treatment, "Ace Adherent" was applied to obtain satisfactory traction. About seventy-two hours after the application a well-circumscribed, erythematous, vesicular, scaly eruption developed over the area where the adherent was applied (Fig. 1). Wet dressing and penicillin ointment were employed to alleviate itching.

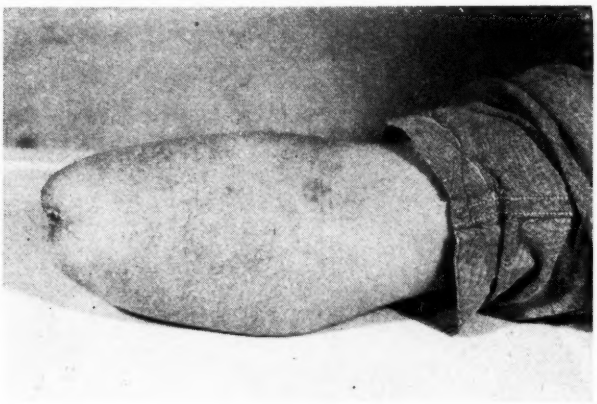

Fig. 1.

When the adherent was reapplied, a similar eruption was produced. The local reaction was followed by a generalized eruption of an urticarial type. After several days the local and generalized eruption began to subside. A patch test performed with the "Ace Adherent" gave a marked reaction necessitating the removal of the test material after four hours. There was a definite erythema and vesiculation at the site of the patch. The patient had no further difficulty after the discontinuance of the "Ace Adherent."

COMMENT

In a large series of amputees in which a variety of traction appliances were used, four cases of dermatitis due to "Ace Adherent" were encountered. A generalized urticarial eruption occurred in only one of these. This appeared in areas distant from the site of the original application of the adherent, and probably was due to absorption of ingredients in the adhesion.

Keil and Bereston[1] have given a comprehensive review of dermatitis due to a transparent adhesive tape. This included a classification of the tapes used, the reactions and the chemistry of the rosins. On inquiry, the manufacturer* stated that the ingredients of "Ace Adherent" were Galex, Venice turpentine, tannic acid, gum camphor and ethyl alcohol. Galex is a highly purified, relatively nonoxidizing rosin. Its chief ingredient is dehydro-abietic acid. The contact dermatitis resulting from the use of "Ace Adherent" is most likely due to this highly purified nonoxidizing rosin known as "Galex" since these acid resins were considered responsible for some cases of contact dermatitis that followed the use of ordinary adhesive tape. Keil[2] believes, however, that the role of abietic acid has been overstressed.

SUMMARY

1. Contact dermatitis due to "Ace Adherent" used in skin traction is reported.

2. Removal of the irritant was quickly followed by complete disappearance of the dermatitis.

3. The cause of the dermatitis was probably a type of dehydrogenated rosin, known as "Galex."

4. In cases in which dermatitis occurs about the amputate stump, adhesive traction material should be considered a likely sensitizing agent.

REFERENCES

1. Keil, H., and Bereston, E. S.: Dermatitis Due to Transparent Adhesive Tape, Arch. Dermat. & Syph. 45: 1052, 1942.
2. Keil, H.: Personal communication.

*Becton, Dickinson & Co., Rutherford, N. J.

American Academy of Allergy

NEWS AND NOTES

Southeastern Allergy Association

On Nov. 1, 1945, a group of doctors met in Charleston, S. C., for the purpose of organizing an allergy association in the southeast. This regional association would include all those doctors in Virginia, North and South Carolina, Georgia, Florida, Tennessee, and Alabama who are interested in allergy.

It was decided to hold the first meeting in Atlanta, Ga., in March, 1946. Plans for this meeting are nearing completion and will be given briefly now.

The meeting is to be held at the Atlanta-Biltmore Hotel, Atlanta, Ga., on Saturday, March 30, and Sunday, March 31.

Business meeting will begin at 10 A.M. Saturday, with Dr. Hal McCluney Davison presiding. There is considerable business to be presented, and the entire morning has been given to this.

Luncheon at noon will be followed by a scientific session with the following program:

1. "Contact Allergy," by Dr. Oscar Swineford.
2. "Headaches," by Dr. William Crowe.
3. "Preparation of Extracts," by Dr. Edna Pennington.

There will be a banquet at night which the Atlanta men are planning. (Dinner clothes will be optional for the banquet.)

The Sunday morning session, to begin at 10 A.M., will include:

1. "The Relationship Between Immédiate and Delayed Skin Reactions," by Dr. John Jacobs.
2. "Allergy in Childhood," by Dr. Susan Dees.
3. "Allergic Rhinitis," by Dr. Randolph Graham.

Each paper will have two discussants and then will be thrown open to all. These discussants will be named in a later bulletin.

This meeting is open to everyone interested in allergy regardless of the type practice one has.

Pollen Sampling Device

During the summer of 1945, a pollen sampling device, devised by O. C. Durham, was thoroughly tested by the National Pollen Survey Committee of the American Academy of Allergy aided by about a dozen collaborators in different parts of the country. With minor modifications, this pollen slide shelter has been accepted by the National Pollen Survey Committee and has been released for manufacture to the Wilkens-Anderson Company of 111 North Canal Street, Chicago 6, Ill. All royalties having been waived, this instrument will sell at $16.00. These shelters will be available for use during the ragweed season of 1946 provided orders for them are placed before April 30. A detailed description of the instrument, as well as the exposure, counting, and staining methods which are recommended by the National Pollen Survey Committee will appear in a committee report in an early issue of The Journal of Allergy.

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1940 **Marton, Samuel,** 333 West End Ave., New York 23, N. Y.
b 1900. Premed., Fordham 1920; M.D., U. Md. 1924; Assoc. Att. Phys. and Chief Dept. Allergy, Jewish Memorial Hosp.; F. A.C.A.; A.M.A.

1940 **Marquis, Dean W.,** 102nd St., Virginia Beach, Va.

1942 **Medivetsky, Harold E.,** 217 So. Union St., Burlington, Vt.
b 1908. B.S., U. Vt. 1929; M.D., 1932; Att. Allergy, Mary Fletcher Hosp.; Consult. Allergy, Bishop De Goesbriand and Fanny Allen Hosps.; In charge Allergy, Clin. U. Disp.; Instr., Clin. Med., U. Vt.; M., New England Ped. Soc.

1941 **Messer, William,** 1548 49th St., Brooklyn 19, N. Y.
b 1902. Premed., Columbia U.; M.D., L. I. Med. Coll. 1925; Cert. in Intern. Med. 1943; Asst. Chief Child. Allergy and Consult. Serv., Mt. Sinai Hosp.; Asst. Phys. Intern. Med., Israel Zion Hosp.

1939 **Metzger, Frank Curry,** 914 Citizens Bldg., Tampa 2, Fla.
b 1892. Premed. U. Cinn.; M.D., 1915; Chief Staff Allergy, Tampa Munic. Hosp., Staff St. Joseph's Hosp.; A.M.A.; M.A.C.A.

1944 **Miller, Harry Irwin,** 3401 Fifth Ave., Pittsburgh 13, Pa.
b 1906. B.S., U. Pittsburgh 1926; M.D., 1929; Sr. Asst., Dept. Med., Montefiore Hosp.; Instr. Med., U. Pittsburgh; A.M.A.; Alpha Omega Alpha.

1942 **Miller, Jerome,** 1920 Pine St., Philadelphia 3, Pa.
b 1906. Premed., U. Pa. 1928; M.D., Temple U. 1932; Mt. Sinai Hosp; Chief Allergy (Private), Union Health Centre; Temple U. Med. Sch.; M., Phila. Allergy Soc.

1944 **Mitchell, John Harrington,** 21 East State St., Columbus 15, Ohio.
b 1904. M.D., Ohio State U. 1928; University, Mt. Carmel, Grant, and White Cross Hosps.; Asst. Prof. Med., Ohio State U.; F.A.C.A.

1944 **Mitchell, William F.,** 21 East State St., Columbus 15, Ohio.

1938 **Moore, Merle Wayland,** Medical Arts Bldg., Portland 5, Ore.
b 1895. B.S., U. Oregon 1920; M.D., Jefferson Med. Coll. 1924; Providence and Multnomah Co. Hosps.; Allergy Clin., U. Oregon Med. Sch.; Assoc., Med. U. Oregon Med. Sch.; F.A.C.P.; A.M.A.; A.C.A.; N. Pacific Soc. Intern. Med.

1941 **Morse, Charles Orrin,** 261 Hamilton, Palo Alto, Calif.
b 1898. A.B., U. Calif. and Stanford U. 1929; M.D., U. Colorado 1933; Stanford U. Sch. Health, 1935-1944.

1942 **Mosko, Milton M.,** 5431 Cornell Ave., Chicago 40, Ill.
b 1910. B.S., U. Ill. 1930; M.D., 1933; Maj., M.C., A.A.F.; Cert. in Intern Med. 1944 and Allergy 1944; F. Sigma Xi; A.M.A.; Chicago Allergy Soc.

1939 **Mulligan, Ralph Mitchell,** 18 North Eleventh St., Reading, Pa.
b 1904. B.S., High Point Coll., N. C., 1930; M.D., Med. Coll. Va. 1934; Chief Allergy and Dermat., St. Joseph's Hosp., Reading; F.A.C.A.; M., Phila. Allergy Soc.

1942 **Myers, William A.,** 814 E. Market St., York, Pa.

1944 **Nozik, Benjamin,** 2405 Fenwood Rd., University Heights, Ohio.
b 1903. B.A., Western Reserve U. 1925; M.D., 1928; Capt., M.C.; Clinician, Div. of Allergy, Mt. Sinai Hosp.; F.A.M.A.; A.C.A.; Alpha Omega Alpha; Cleveland Allerg. Soc., Sec. 1938, Pres. 1939.

1939 **Parsons, John Warner,** 1010 N. Calvert St., Baltimore, Md.
b 1904. A.B., Johns Hopkins 1925; M.D., 1930; Lt. Comdr., M.C., U.S.N.R.; Asst. Vis. Phys., Johns Hopkins Hosp.; Instr. Med., Johns Hopkins Med. Sch.

1941 **Pennypacker, Charles S.,** 111 E. Montgomery Ave., Ardmore, Pa.
b 1910. B.S., Haverford 1931; M.D., U. Pa. 1935; Capt. M.C., A.U.S.; Chief Gen. Med. Sec., Chief Allergy Clin., Rhoads Gen. Hosp., Utica, N. Y.; F., Phila Coll. Phys.; Phila. Allergy Soc.

1941 **Peters, Alexander Monroe,** 45 N. 11th St., Allentown, Pa.
b 1898. Premed., Bucknell U. 1921; M.D., Jefferson Med. Coll. 1924; Chief Ped. and Allergy, Allentown Hosp.; Clin. Asst. Allergy, Jefferson Hosp., O.P.D.; A.M.A.; M., Phila. Allergy Soc.; Pres. Fleet Lehigh Co., Med. Soc., 1944.

1940 **Peters, Frank Hart,** 1009 Park Ave., New York 28, N. Y.
b 1896. Premed., Columbia U.; M.D., 1920; Att. Phys., Bellevue Hosp.; Asst. Att. Phys., New York Hosp.; Asst. Prof. Clin. Med., Cornell Med. Coll.; F.A.C.P.; N. Y. Acad. Med.; A.M.A.

1940 **Pipes, David M.,** 217 Jefferson Bldg., Greensboro, N. C.
b 1905. B.A., Louisiana State U., Southwestern Memphis 1928; M.D., Tulane 1934; F.A.C.A.

1943 **Prigal, Samuel Jeremiah,** 55 Park Ave., New York City 15, N. Y.
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1944 **Quintero, Jose M.,** San Lazaro 464, 3er, Piso, Havana, Cuba, 94

1944 **Randolph, Theron Grant,** 700 N. Michigan Ave., Chicago 11, Ill.
b 1906. A.B., Hillsdale Coll. 1929; M.D., U. Mich. 1933; Cert. in Intern. Med. 1944; Passavant Memorial Hosp.; Instr. in Med., Northwestern U. Med. Sch.; A.M.A.; Central Soc. for Clin. Research; A. Fed. Clin. Research; Chicago Soc. Allerg.

1941 **Raynolds, Arthur Hidden,** 50 E. 72nd St., New York 21, N. Y.
b 1900. A.B., Princeton 1922; M.D., Columbia U. 1926; Capt., M.C., A.U.S.; Phys., O.P.D., N.Y. Hosp.; Assoc. Vis. Phys., Chief Allergy Clin., Lincoln Hosp.; Instr. Med., Cornell Med. Sch.; A.M.A.; N. Y. Acad. Med.

(To be continued.)

Book Reviews

Familial Non-Reaginic Food Allergy. Arthur F. Coca, M.D., Second Edition, Springfield, 1945, Charles C Thomas, pp. 185.

The fact that this is the second addition of this book testifies to considerable interest in the theories of this distinguished author. In the preface he concedes a wide divergence between his findings and accepted medical dogma. He admits that his concept is of a sufficiently revolutionary nature to explain the hesitation of experienced medical specialists to try the methods of diagnosis and treatment described and admits also that only two have seriously asked his help.

The author states that the most common cause of variation of pulse rate which is a constant, physiological to each individual, is familial nonreaginic food allergy or idioblapsis. He contends that upwards of 80 per cent of the white population are hereditarily affected and that this disorder is the most important primary cause of noninfectious disease.

When one seeks proof of these statements in the text, or a convincing explanation of the mechanism involved, he remains unsatisfied. To be sure, if one accepts disorders as overweight, psychic depression, gastrointestinal bleeding, and physical tiredness (second most common symptom), among some thirty other symptoms as due to this form of food allergy, a good many people would be involved.

It is only fair to state that the reviewer has had little experience with the methods described but would be tempted to try them if the author, who has been so meticulous in his immunological investigation, would direct as inquiring an attitude toward his clinical studies.